- # Vitamin D modulates the content of inflammatory microRNAs in extracellular vesicles from human adipocyte cells in inflammatory context

Type de document	Article de revue
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Auteur	Stéphane Robert
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Auteur	Lourdes Mounien
Résumé	Inflammation of adipose tissue is a contributing factor to many chronic diseases associated with obesity. We previously showed that micronutrients such as vitamin D (VD) limited this metabolic inflammation by decreasing inflammatory markers expression including miR-155 (microRNA-155) or miR-146a in different in vitro and in vivo models. These miRNAs could be incorporated into extracellular vesicles (EVs) in order to modulate the activity of target cells. Nevertheless, the role of VD on the miRNAs contained in EVs from adipose tissue in inflammatory conditions remains unclear. In this study, we used a human model of SGBS (Simpson-Golabi-Behmel syndrome) adipocytes preincubated with 1,25(OH)2D (the active form of VD) before an inflammatory stress with tumor necrosis factor α (TNFα). First, we confirmed by quantitative PCR that the expression of classical inflammatory factors (TNFα and chemokine ligand 2 [CCL2/MCP1]), miR-146a, and miR-155 was increased significantly under inflammatory conditions in SGBS cells and that VD prevented this up-regulation. Secondly, transmission electron microscope imaging of EVs preparations in supernatant allowed visualization of small and large vesicles under these conditions. Then, EVs were obtained with isolation kit and the expression of miR-155 and miR-146a were measured. The expression of miR-155 under TNFα effect was increased in EVs while miR-146a was not detected. Moreover, we also showed that the TNFα-mediated expression of miR-155 in EVs was significantly reduced by a VD pre-incubation of cells. Using miRNA PCR array, we also identified 33 miRNAs, organized in 5 clusters that were differentially regulated by TNFα and VD. Bioinformatic analysis of biological pathways revealed that the different miRNAs targeting genes that are involved in important cell process such as the regulation of transcription or protein phosphorylation. In conclusion, these results support for the first time that VD modulated the expression of miRNAs

	in EVs from adipocytes, which could represent a new mechanism of regulation of inflammation by micronutrients.
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Langue	eng
Catalogue de bibl.	PubMed
Extra	PMID: 39887543 PMCID: PMC11779547
Volume	51
Pages	e70003
Publication	BioFactors (Oxford, England)
DOI	[10.1002/biof.70003](https://doi.org/10.1002/biof.70003)
Numéro	1
Abrév. de revue	Biofactors
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- **Marqueurs :**
  - Adipocytes
  - Arrhythmias, Cardiac
  - extracellular vesicles
  - Extracellular Vesicles
  - Gene Expression Regulation
  - Genetic Diseases, X-Linked
  - Gigantism
  - Heart Defects, Congenital
  - human adipocyte
  - Humans
  - inflammation
  - Inflammation
  - Intellectual Disability
  - microRNAs
  - MicroRNAs
  - Tumor Necrosis Factor-alpha
  - Vitamin D

  Pièces jointes

  - PubMed entry

- ## Sex-specific NLRP3 activation in neutrophils promotes neutrophil recruitment and NETosis in the murine model of diffuse alveolar hemorrhage

Type de document	Article de revue
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Auteur	William Chan
Auteur	Lukas Heger
Auteur	Nicolas Schommer
Auteur	Pierre Cunin
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Auteur	Peter A. Nigrovic
Auteur	Bruce Ewenstein
Auteur	Denisa Wagner
Résumé	Diffuse alveolar hemorrhage (DAH) is a life-threatening complication of systemic lupus erythematosus and small vessel vasculitis. We previously showed that neutrophil extracellular traps (NETs) were associated with the pathogenesis of pristane-induced DAH and demonstrated that neutrophil NOD-like receptor family pyrin domain containing 3 (NLRP3) inflammasome assembly participated in NET generation under sterile stimulation. We investigated whether NLRP3 inflammasome assembly in neutrophils may drive pulmonary NETosis in a mouse model of pristane-induced DAH.C57BL/6J mice received a single intraperitoneal injection of 0.5mL of pristane. Neutrophil NLRP3 inflammasome assembly and NETs were characterized by immunofluorescence staining of apoptosisassociated speck-like protein a CARD (ASC), co-staining of DNA, and citrullinated histones, respectively. Clinical status of mice was assessed 11 days after pristane injection by measurement of arterial oxygen saturation and of weight loss; severity of lung injury was determined using a quantification score from hematoxylin-eosin-stained slides.Pristane induced ASC speck formation in neutrophils and we confirmed that NLRP3 inflammasome was involved in NET generation after pristane stimulation in vitro. NLRP3 deficiency reduced the severity of pristane-induced DAH in female, but not male mice. Interestingly, NLRP3 deficiency reduced the number of neutrophils and NETs in the lungs of females compared to males.Our results suggest a link between female sex-specific NLRP3 inflammasome activation and subsequent pulmonary NETosis in the development of pristane-induced DAH. Therefore, we identified NLRP3 inflammasome as a potential new therapeutic target in this severe complication of pro-female autoimmune disease for which specific inhibitors of NLRP3 are currently developed.
Date	2024-11-04
Langue	English
Catalogue de bibl.	Frontiers

URL	https://www.frontiersin.org/journals/immunology/articles/10.3389/fimmu.2024.1466234/abstract
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Extra	Publisher: Frontiers
Volume	15
Publication	Frontiers in Immunology
DOI	10.3389/fimmu.2024.1466234
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- **Marqueurs :**
  - Diffuse alveolar hemorrhage
  - murine model
  - neutrophil extracellular traps
  - NLRP3 inflammasome
  - sexspecific
- # Role of the NLRP3 inflammasome in myocarditis induced by immune checkpoint inhibitors cancer immunotherapy

Type de document	Article de revue
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Auteur	Isaure Firoaguer
Auteur	Stéphanie Simoncini
Auteur	Stéphane Robert
Auteur	Claire El Yazidi
Auteur	Frédérique Magdinier
Auteur	Denis Puthier
Auteur	Franck Thuny
Auteur	Jennifer Cautela
Auteur	Nathalie Lalevée
Résumé	Introduction The inflammasome NLRP3 is involved in the inflammatory processes of several cardiac diseases. Recently, GBP5 and 6 transcripts have been found to be specifically deregulated in immune-related

myocarditis, but the mechanism of action remains unclear. Cardiomyocyte dysfunction during the cardiotoxic reaction probably results from the combined action of cytokines secreted by T lymphocytes reactivated by ICIs and inflammatory molecules released by endocardial and vascular endothelial cells. Our hypothesis is that cardiac dysfunction in immune-mediated myocarditis is linked to activation of the NLRP3 inflammasome in cardiac cells in this inflammatory context. Objective Our aim is to unravel the regulatory mechanisms of the NLRP3 inflammasome in response to cytokines known to be secreted during ICI-related myocarditis, and to characterise the role of paracrine effects of endothelial cells in cardiomyocyte dysfunction. Method hiPSC-derived cardiomyocytes (hiPSC-CM) and endothelial cells (hiPSC-EC) were stimulated by different inflammatory cytokines (IFN-γ, RANTES, Granzyme B and IL-1β). We studied several groups: healthy individual (1 clone from 1 individual), melanoma patients who reported immuno-mediated myocarditis (13 clones from 5 patients), and melanoma patients who did not report cardiotoxicity after immunotherapy (7 clones from 3 patients). Results IFN-γ affects the viability of cardiac cells by activating the JAK/STAT inflammatory pathway, and by overexpressing NLRP3 inflammasome transcripts such as nlrp3, nlrc5 and caspase-1. This effect is associated to overexpression of the MHC and PD-L1 proteins, as described in humans. IFN-γ alone did not induce significant differences between groups on these targets. We have developed a flow cytometry multiplexing protocol to characterise apoptosis associated with caspase activity, in particular NLRP3 inflammasome-associated caspase-1, metabolic deregulation and oxidative stress. The results are currently being analysed after stimulation by inflammatory cytokines IFN-γ, RANTES, Granzyme B and IL-1β. Conclusion hiPSC-CM and hiPSC-EC respond to IFN-γ by activating inflammatory pathways, in particular the NLRP3 inflammasome, leading to cell death. Our work unravels the mechanisms associated with cardiotoxicity, triggered by inflammatory cytokines released during the cardiotoxic response to ICIs, thus clarifying the role of the two cardiac cell types in the cardiac dysfunction observed in immuno-mediated myocarditis in patients.

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URL	https://www.sciencedirect.com/science/article/pii/S1875213624001347
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Volume	117
Pages	S191
Publication	Archives of Cardiovascular Diseases
Collection	Printemps de la cardiologie 2024
DOI	10.1016/j.acvd.2024.05.062
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Abrév. de revue	Archives of Cardiovascular Diseases

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- **Pièces jointes**
  - ScienceDirect Snapshot

- # Endothelial PTP1B Deletion Promotes VWF Exocytosis and Venous Thromboinflammation

Type de document	Article de revue
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Auteur	Stephane Robert
Auteur	Denise Pedrosa
Auteur	Klytaimnistra Kiouptsi
Auteur	Kateryna Moiko
Auteur	Mathias Wagner
Auteur	Felix Mahfoud
Auteur	Philippe Poncelet
Auteur	Thomas Münzel
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Auteur	Christoph Reinhardt
Auteur	Laurence Panicot-Dubois
Auteur	Christophe Dubois
Auteur	Katrin Schäfer
Résumé	BACKGROUND: Endothelial activation promotes the release of procoagulant extracellular vesicles and inflammatory mediators from specialized storage granules. Endothelial membrane exocytosis is controlled by phosphorylation. We hypothesized that the absence of PTP1B (protein tyrosine phosphatase 1B) in endothelial cells promotes venous thromboinflammation by triggering endothelial membrane fusion and exocytosis. METHODS: Mice with inducible endothelial deletion of PTP1B (End.PTP1B-KO) underwent inferior vena cava ligation to induce stenosis and venous thrombosis. Primary endothelial cells from transgenic mice and human umbilical vein endothelial cells were used for mechanistic studies. RESULTS: Vascular ultrasound and histology showed significantly larger venous thrombi containing higher numbers of Ly6G (lymphocyte antigen 6 family member G)-positive neutrophils in mice with endothelial PTP1B deletion, and intravital microscopy confirmed the more pronounced neutrophil recruitment following inferior vena cava ligation. RT2 PCR profiler array and

immunocytochemistry analysis revealed increased endothelial activation and adhesion molecule expression in primary End.PTP1B-KO endothelial cells, including CD62P (P-selectin) and VWF (von Willebrand factor). Pretreatment with the NF-κB (nuclear factor kappa B) kinase inhibitor BAY11-7082, antibodies neutralizing CD162 (P-selectin glycoprotein ligand-1) or VWF, or arginylglycylaspartic acid integrin-blocking peptides abolished the neutrophil adhesion to End.PTP1B-KO endothelial cells in vitro. Circulating levels of annexin V+ procoagulant endothelial CD62E+ (E-selectin) and neutrophil (Ly6G+) extracellular vesicles were also elevated in End.PTP1B-KO mice after inferior vena cava ligation. Higher plasma MPO (myeloperoxidase) and Cit-H3 (citrullinated histone-3) levels and neutrophil elastase activity indicated neutrophil activation and extracellular trap formation. Infusion of End.PTP1B-KO extracellular vesicles into C57BL/6J wild-type mice most prominently enhanced the recruitment of endogenous neutrophils, and this response was blunted in VWF-deficient mice or by VWF-blocking antibodies. Reduced PTP1B binding and tyrosine dephosphorylation of SNAP23 (synaptosome-associated protein 23) resulting in increased VWF exocytosis and neutrophil adhesion were identified as mechanisms, all of which could be restored by NF-κB kinase inhibition using BAY11-7082. CONCLUSIONS: Our findings show that endothelial PTP1B deletion promotes venous thromboinflammation by enhancing SNAP23 phosphorylation, endothelial VWF exocytosis, and neutrophil recruitment.

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Langue	eng
Catalogue de bibl.	PubMed
Extra	PMID: 38563147
Publication	Circulation Research
DOI	10.1161/CIRCRESAHA.124.324214
Abrév. de revue	Circ Res
ISSN	1524-4571
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- **Marqueurs :**
  - extracellular vesicles
  - neutrophils
  - endothelial cells
  - venous thrombosis
  - von Willebrand factor

Pièces jointes

- PubMed entry

- ## A compendium of single extracellular vesicle flow cytometry

Type de document	Article de revue
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Auteur	Michel Bremer
Auteur	Michael Cimorelli
Auteur	Françoise Dignat-George
Auteur	Bernd Giebel
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Auteur	An Hendrix
Auteur	Martine Kuiper
Auteur	Romaric Lacroix
Auteur	Joanne Lannigan
Auteur	Ton G. van Leeuwen
Auteur	Estefanía Lozano-Andrés
Auteur	Shoaib Rao
Auteur	Stéphane Robert
Auteur	Leonie de Rond
Auteur	Vera A. Tang
Auteur	Tobias Tertel
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Auteur	Jennifer C. Jones
Auteur	Rienk Nieuwland
Auteur	Edwin van der Pol
Résumé	Flow cytometry (FCM) offers a multiparametric technology capable of characterizing single extracellular vesicles (EVs). However, most flow cytometers are designed to detect cells, which are larger than EVs. Whereas cells exceed the background noise, signals originating from EVs partly overlap with the background noise, thereby making EVs more difficult to detect than cells. This technical mismatch together with complexity of EV-containing fluids causes limitations and challenges with conducting, interpreting and reproducing EV FCM experiments. To address and overcome these challenges, researchers from the International Society for Extracellular Vesicles (ISEV), International Society for Advancement of Cytometry (ISAC), and the International Society on Thrombosis and Haemostasis (ISTH) joined forces and initiated the EV FCM working group. To improve the interpretation, reporting, and reproducibility of future EV FCM data, the EV FCM

working group published an ISEV position manuscript outlining a framework of minimum information that should be reported about an FCM experiment on single EVs (MIFlowCyt-EV). However, the framework contains limited background information. Therefore, the goal of this compendium is to provide the background information necessary to design and conduct reproducible EV FCM experiments. This compendium contains background information on EVs, the interaction between light and EVs, FCM hardware, experimental design and preanalytical procedures, sample preparation, assay controls, instrument data acquisition and calibration, EV characterization, and data reporting. Although this compendium focuses on EVs, many concepts and explanations could also be applied to FCM detection of other particles within the EV size range, such as bacteria, lipoprotein particles, milk fat globules, and viruses.

Date	2023
Langue	en
Catalogue de bibl.	Wiley Online Library
URL	http://onlinelibrary.wiley.com/doi/abs/10.1002/jev2.12299
Consulté le	20/02/2023 11:42:21
Extra	_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1002/jev2.12299
Volume	12
Pages	e12299
Publication	Journal of Extracellular Vesicles
DOI	10.1002/jev2.12299
Numéro	2
ISSN	2001-3078
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- **Marqueurs :**
    - extracellular vesicles
    - microparticles
    - standardization
    - nanoparticles
    - flow cytometry
    - calibration
    - MIFlowCyt-EV

Pièces jointes

- Full Text PDF
- Snapshot

- # Macrophage IL-1β-positive microvesicles exhibit thrombo-inflammatory properties and are detectable in patients with active juvenile idiopathic arthritis

Type de document	Article de revue
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Auteur	Richard Bachelier
Auteur	Laurent Arnaud
Auteur	Stéphane Robert
Auteur	Marie Lagarde
Auteur	Romain Muller
Auteur	Edwige Tellier
Auteur	Yéter Kara
Auteur	Aurélie Leroyer
Auteur	Catherine Farnarier
Auteur	Loris Vallier
Auteur	Corinne Chareyre
Auteur	Karine Retornaz
Auteur	Anne-Laure Jurquet
Auteur	Tu-Anh Tran
Auteur	Romaric Lacroix
Auteur	Françoise Dignat-George
Auteur	Gilles Kaplanski
Résumé	ObjectiveIL-1β is a leaderless cytokine with poorly known secretory mechanisms that is barely detectable in serum of patients, including those with an IL-1β-mediated disease such as systemic juvenile idiopathic arthritis (sJIA). Leukocyte microvesicles (MVs) may be a mechanism of IL-1β secretion. The first objective of our study was to characterize IL-1β-positive MVs obtained from macrophage cell culture supernatants and to investigate their biological functions in vitro and in vivo. The second objective was to detect circulating IL-1β-positive MVs in JIA patients.MethodsMVs were purified by serial centrifugations from PBMCs, or THP-1 differentiated into macrophages, then stimulated with LPS ± ATP. MV content was analyzed for the presence of IL-1β, NLRP3 inflammasome, caspase-1, P2X7 receptor, and tissue factor (TF) using ELISA, Western blot, or flow cytometry. MV biological properties were studied in vitro by measuring VCAM-1, ICAM-1, and E-selectin expression after HUVEC co-culture and factor-Xa generation test was realized. In vivo, MVs' ability to recruit leukocytes in a murine model of peritonitis was evaluated. Plasmatic IL-1β-positive MVs were studied ex vivo in 10 active JIA patients using flow cytometry.ResultsTHP-1-derived macrophages stimulated with

	LPS and ATP released MVs, which contained NLRP3, caspase-1, and the 33-kDa precursor and 17-kDa mature forms of IL-1β and bioactive TF. IL-1β-positive MVs expressed P2X7 receptor and released soluble IL-1β in response to ATP stimulation in vitro. In mice, MVs induced a leukocyte peritoneal infiltrate, which was reduced by treatment with the IL-1 receptor antagonist. Finally, IL-1β-positive MVs were detectable in plasma from 10 active JIA patients.ConclusionMVs shed from activated macrophages contain IL-1β, NLRP3 inflammasome components, and TF, and constitute thrombo-inflammatory vectors that can be detected in the plasma from active JIA patients.
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Catalogue de bibl.	Frontiers
URL	https://www.frontiersin.org/articles/10.3389/fimmu.2023.1228122
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Volume	14
Publication	Frontiers in Immunology
ISSN	1664-3224
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- **Pièces jointes**
  - Full Text PDF
- ## Immune thrombotic thrombocytopenic purpura plasmas induce calcium- and IgG-dependent endothelial activation: correlations with disease severity

Type de document	Article de revue
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Auteur	Raphaël Cauchois
Auteur	Julien Faccini
Auteur	Marie Lagarde
Auteur	Marion Brun
Auteur	Philippe Robert
Auteur	Stéphane Robert
Auteur	Richard Bachelier
Auteur	Pascale Poullin
Auteur	Elien Roose
Auteur	Karen Vanhoorelbeke

Auteur	Paul Coppo
Auteur	Françoise Dignat-George
Auteur	Gilles Kaplanski
Résumé	Immune-mediated thrombotic thrombocytopenic purpura (iTTP) is characterized by a severe ADAMTS13 deficiency due to the presence of anti-ADAMTS13 autoantibodies, with subsequent accumulation of circulating ultra-large von Willebrand Factor (VWF) multimers. The role of endothelial cell activation as a trigger of the disease has been suggested in animal models but remains to be demonstrated in humans. We prospectively obtained plasma from the first plasma exchange of 25 patients during iTTP acute phase. iTTP but not control plasma, induced a rapid VWF release and P-selectin exposure on dermal human micro-vascular endothelial cell (HMVEC-d) surface, associated with angiopoietin-2 and endothelin-1 secretion, consistent with Weibel-Palade bodies exocytosis. Calcium (Ca2+) blockade significantly decreased VWF release, whereas iTTP plasma induced a rapid and sustained Ca2+ flux in HMVEC-d which correlated in retrospect, with disease severity and survival in 62 iTTP patients. F(ab)'2 fragments purified from the immunoglobulin G (IgG) fraction of iTTP plasma mainly induced endothelial cell (EC) activation with additional minor roles for circulating free heme and nucleosomes, but not for complement. Furthermore, two anti-ADAMTS13 monoclonal antibodies purified from iTTP patient B cells, but not serum from hereditary TTP, induced endothelial Ca2+ flux associated with Weibel-Palade bodies exocytosis in vitro, whereas inhibition of endothelial ADAMTS13 expression using small interference RNA, significantly decreased the stimulating effects of iTTP IgG. In conclusion, Ca2+-mediated endothelial cell activation constitutes a second "hit" of iTTP, is correlated with the severity of the disease and may constitute a possible therapeutic target.
Date	2022-12-01
Langue	eng
Titre abrégé	Immune thrombotic thrombocytopenic purpura plasmas induce calcium- and IgG-dependent endothelial activation
Catalogue de bibl.	PubMed
Extra	PMID: 36453103
Publication	Haematologica
DOI	[10.3324/haematol.2022.280651](https://doi.org/10.3324/haematol.2022.280651)
Abrév. de revue	Haematologica
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- ## Pièces jointes

- PubMed entry
- Texte intégral

- ## Granulocyte microvesicles with a high plasmin generation capacity promote clot lysis and improve outcome in septic shock

Type de document	Article de revue
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Auteur	Pierre Esnault
Auteur	Mathilde Dacos
Auteur	Amandine Bonifay
Auteur	Nicolas Macagno
Auteur	Karim Harti Souab
Auteur	Corinne Chareyre
Auteur	Coralie Judicone
Auteur	Diane Frankel
Auteur	Stephane Robert
Auteur	Sami Hraiech
Auteur	Marie-Christine Alessi
Auteur	Philippe Poncelet
Auteur	Jacques Albanese
Auteur	Françoise Dignat-George
Auteur	Romaric Lacroix
Résumé	Microvesicles (MVs) have previously been shown to exert profibrinolytic capacity, which is increased in patients with septic shock (SS) with a favorable outcome. We therefore hypothesized that the plasmin generation capacity (PGC) could confer to MVs a protective effect supported by their capacity to lyse a thrombus, and we investigated the mechanisms involved. Using a MV-PGC kinetic assay, ELISA and flow cytometry, we found that granulocyte MVs (Gran-MVs) from SS patients display a heterogeneous PGC profile driven by the uPA (urokinase)/uPAR system. In vitro, these MVs lyse a thrombus according to their MV-PGC levels in a uPA/uPAR-dependent manner, as shown in a fluorescent clot lysis test and a lysis front retraction assay. Fibrinolytic activators conveyed by MVs contribute to approximately 30% of the plasma plasminogenolytic capacity of SS patients. In a murine model of SS, the injection of high PGC Gran-MVs significantly improved mouse survival and reduced the number of thrombi in vital organs. This was associated with a modification of the mouse coagulation and fibrinolysis properties toward a more fibrinolytic profile. Interestingly, mouse survival was not improved when soluble uPA was injected. Finally, using a multiplex array on plasma from SS patients, we found that neutrophil elastase correlates

with the effect of high-PGC-capacity plasma and modulates the Gran-MV plasmin generation capacity by cleaving uPA-PAI-1 complexes. In conclusion, we show that high PGC level displayed by Gran-MVs reduce thrombus formation and improve survival conferring to Gran-MVs a protective role in a murine model of sepsis.

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Langue	eng
Catalogue de bibl.	PubMed
Extra	PMID: 35026004
Pages	blood.2021013328
Publication	Blood
DOI	10.1182/blood.2021013328
Abrév. de revue	Blood
ISSN	1528-0020
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- **Pièces jointes**
    - PubMed entry
- # Soluble CD146 as a Potential Target for Preventing Triple Negative Breast Cancer MDA-MB-231 Cell Growth and Dissemination

Type de document	Article de revue
Auteur	Akshita Sharma
Auteur	Ahmad Joshkon
Auteur	Aymen Ladjimi
Auteur	Waël Traboulsi
Auteur	Richard Bachelier
Auteur	Stéphane Robert
Auteur	Alexandrine Foucault-Bertaud
Auteur	Aurélie S. Leroyer
Auteur	Nathalie Bardin
Auteur	Indumathi Somasundaram
Auteur	Marcel Blot-Chabaud
Résumé	Background: Triple Negative Breast Cancers (TNBC) are the most aggressive breast cancers and lead to poor prognoses. This is due to a high resistance to therapies, mainly because of the presence of Cancer Stem Cells (CSCs). Plasticity, a feature of CSCs, is acquired through the Epithelial to Mesenchymal Transition (EMT), a process that has

been recently shown to be regulated by a key molecule, CD146. Of interest, CD146 is over-expressed in TNBC. Methods: The MDA-MB-231 TNBC cell line was used as a model to study the role of CD146 and its secreted soluble form (sCD146) in the development and dissemination of TNBC using in vitro and in vivo studies. Results: High expression of CD146 in a majority of MDA-MB-231 cells leads to an increased secretion of sCD146 that up-regulates the expression of EMT and CSC markers on the cells. These effects can be blocked with a specific anti-sCD146 antibody, M2J-1 mAb. M2J-1 mAb was able to reduce tumour development and dissemination in a model of cells xenografted in nude mice and an experimental model of metastasis, respectively, in part through its effects on CSC. Conclusion: We propose that M2J-1 mAb could be used as an additional therapeutic approach to fight TNBC.

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Langue	en
Catalogue de bibl.	www.mdpi.com
URL	https://www.mdpi.com/1422-0067/23/2/974
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Autorisations	http://creativecommons.org/licenses/by/3.0/
Extra	Number: 2 Publisher: Multidisciplinary Digital Publishing Institute
Volume	23
Pages	974
Publication	International Journal of Molecular Sciences
DOI	10.3390/ijms23020974
Numéro	2
Date d'ajout	17/01/2022 10:38:09
Modifié le	17/01/2022 10:38:09

- **Marqueurs :**
    - CD146
    - treatment
    - triple negative breast cancer

  Pièces jointes

    - Full Text PDF
    - Snapshot

- ## A new strategy to count and sort neutrophil-derived extracellular vesicles: Validation in infectious disorders

Type de document	Article de revue

Auteur	Amandine Bonifay
Auteur	Stéphane Robert
Auteur	Belinda Champagne
Auteur	Paul-Rémi Petit
Auteur	Aude Eugène
Auteur	Corinne Chareyre
Auteur	Anne-Claire Duchez
Auteur	Mélanie Vélier
Auteur	Shirley Fritz
Auteur	Loris Vallier
Auteur	Romaric Lacroix
Auteur	Françoise Dignat-George
Résumé	Newly recognized polymorphonuclear neutrophil (PMNs) functions include the ability to release subcellular mediators such as neutrophil-derived extracellular vesicles (NDEVs) involved in immune and thrombo-inflammatory responses. Elevation of their plasmatic level has been reported in a variety of infectious and cardiovascular disorders, but the clinical use of this potential biomarker is hampered by methodological issues. Although flow cytometry (FCM) is currently used to detect NDEVs in the plasma of patients, an extensive characterization of NDEVs has never been done. Moreover, their detection remains challenging because of their small size and low antigen density. Therefore, the objective of the present study was first to establish a surface antigenic signature of NDEVs detectable by FCM and therefore to improve their detection in biological fluids by developing a strategy allowing to overcome their low fluorescent signal and reduce the background noise. By testing a large panel of 54 antibody specificities already reported to be positive on PMNs, we identified a profile of 15 membrane protein markers, including 4 (CD157, CD24, CD65 and CD66c) never described on NDEVs. Among them, CD15, CD66b and CD66c were identified as the most sensitive and specific markers to detect NDEVs by FCM. Using this antigenic signature, we developed a new strategy combining the three best antibodies in a cocktail and reducing the background noise by size exclusion chromatography (SEC). This strategy allowed a significant improvement in NDEVs enumeration in plasma from sepsis patients and made it feasible to efficiently sort NDEVs from COVID-19 patients. Altogether, this work opens the door to a more valuable measurement of NDEVs as a potential biomarker in clinical practice. A similar strategy could also be applied to improve detection by FCM of other rare subpopulations of EVs generated by tissues with limited access, such as vascular endothelium, cancer cells or placenta.
Date	2022
Langue	en
Titre abrégé	A new strategy to count and sort neutrophil-derived extracellular vesicles

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URL	https://onlinelibrary.wiley.com/doi/abs/10.1002/jev2.12204
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Extra	_eprint: https://onlinelibrary.wiley.com/doi/pdf/10.1002/jev2.12204
Volume	11
Pages	e12204
Publication	Journal of Extracellular Vesicles
DOI	10.1002/jev2.12204
Numéro	4
ISSN	2001-3078
Date d'ajout	01/04/2022 15:43:11
Modifié le	01/04/2022 15:43:11

- **Marqueurs :**
  - extracellular vesicles
  - flow cytometry
  - EVs sorting
  - infectious associated diseases
  - neutrophils
  - size exclusion chromatography

  Pièces jointes

  - Full Text PDF
  - Snapshot

- ## Oral Squamous Cell Carcinoma Is Associated with a Low Thrombosis Risk Due to Storage Pool Deficiency in Platelets

Type de document	Article de revue
Auteur	Pierre Haen
Auteur	Lydie Crescence
Auteur	Diane Mege
Auteur	Alexandre Altié
Auteur	Christophe Dubois
Auteur	Laurence Panicot-Dubois
Résumé	Venous thrombo-embolism (VTE) disease is the second most common cause of mortality in cancer patients, and evaluation and prevention of thrombosis risk is essential. VTE-associated risk varies according to the type of tumor disease. Oral cancer is the most frequent type of head and neck cancer, and it represents approximately 2.1% of all cancers

worldwide. Most tumors are squamous cell carcinomas and are mainly due to tobacco and alcohol abuse. VTE risk associated with oral squamous cell carcinoma (OSCC) is low. However, many studies have shown that OSCC has the following biological features of cancers associated with a high thrombosis risk: modified thrombosis and fibrinolysis mechanisms; strong expression of procoagulant proteins; secretion of procoagulant microparticles; and production of procoagulant cytokines. Using an original mouse model of tongue squamous cell carcinoma, our study aimed to clarify this paradoxical situation. First, we showed that OSCC tumors have a pro-aggregatory phenotype and a high local thrombosis risk. Second, we found that tongue tumor mice do not have an elevated systemic thrombosis risk (the risk of an "at distance" thrombosis event such as lower extremity deep venous thrombosis or pulmonary embolism) and even show a reduction in risk. Third, we demonstrated that tongue tumor mice show a reduction in platelet reactivity, which explains the low systemic thrombosis risk. Finally, we found that tongue tumor mice present granule pool deficiency, thereby explaining the reduction in platelet reactivity and systemic thrombosis risk.

Date	2021-02-24
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 3 PMID: 33668375 PMCID: PMC7996194
Volume	9
Pages	228
Publication	Biomedicines
DOI	10.3390/biomedicines9030228
Numéro	3
Abrév. de revue	Biomedicines
ISSN	2227-9059
Date d'ajout	13/12/2021 10:37:53
Modifié le	13/12/2021 10:37:53

- **Marqueurs :**
  - disorders of platelet function
  - intravital microcopy
  - laser injury
  - oral squamous cancer
  - platelet granules

Pièces jointes

  - PubMed entry
  - Texte intégral

- ## The Interaction of Platelets with Colorectal Cancer Cells Inhibits Tumor Growth but Promotes Metastasis

Type de document	Article de revue
Auteur	Léa Plantureux
Auteur	Diane Mège
Auteur	Lydie Crescence
Auteur	Estelle Carminita
Auteur	Stéphane Robert
Auteur	Sylvie Cointe
Auteur	Nicolas Brouilly
Auteur	Walid Ezzedine
Auteur	Françoise Dignat-George
Auteur	Christophe Dubois
Auteur	Laurence Panicot-Dubois
Résumé	Platelets promote metastasis, however, their role in tumor growth remains controversial. Here, we investigated the effect of platelet interactions with colorectal tumor cells. Platelets extravasated into the tumor microenvironment and interacted with tumor cells in a cadherin-6-dependent manner. The interaction induced platelet spreading, release of their granule content, and the generation of three types of microparticles (iMP) that expressed platelet markers, tumor markers, or both. The presence of iMPs was confirmed in colorectal cancer tissue specimens. Platelets significantly reduced tumor growth and increased intratumoral macrophages. This was mediated by iMP recruitment of macrophages via the chemoattractants RANTES, MIF, CCL2, and CXCL12 and activation of their tumor cell killing capacity through IFNγ and IL4, which led to cell-cycle arrest of tumor cells in a p21-dependent manner. In contrast, in the bloodstream, iMPs activated endothelial cells and platelets and induced epithelial-to-mesenchymal transition of tumor cells, promoting metastasis. Altogether, these results indicate that depending on the environment, local or bloodstream, the consequences of the interactions between platelets and a tumor may promote or prevent cancer progression. SIGNIFICANCE: Tumor cell interaction with platelets produces chimeric extracellular vesicles that suppress primary tumor growth by activating tumor-eliminating macrophages, while promoting metastasis through EMT and endothelial activation.
Date	Jan 15, 2020
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 2

Volume	80
Pages	291-303
Publication	Cancer Research
DOI	10.1158/0008-5472.CAN-19-1181
Numéro	2
Abrév. de revue	Cancer Res.
ISSN	1538-7445
Date d'ajout	13/12/2021 10:36:31
Modifié le	13/12/2021 10:36:31

- **Pièces jointes**
  - PubMed entry
- # MIFlowCyt-EV: a framework for standardized reporting of extracellular vesicle flow cytometry experiments

Type de document	Article de revue
Auteur	Joshua A. Welsh
Auteur	Edwin Van Der Pol
Auteur	Ger J. A. Arkesteijn
Auteur	Michel Bremer
Auteur	Alain Brisson
Auteur	Frank Coumans
Auteur	Françoise Dignat-George
Auteur	Erika Duggan
Auteur	Ionita Ghiran
Auteur	Bernd Giebel
Auteur	André Görgens
Auteur	An Hendrix
Auteur	Romaric Lacroix
Auteur	Joanne Lannigan
Auteur	Sten F. W. M. Libregts
Auteur	Estefanía Lozano-Andrés
Auteur	Aizea Morales-Kastresana
Auteur	Stephane Robert
Auteur	Leonie De Rond
Auteur	Tobias Tertel
Auteur	John Tigges
Auteur	Olivier De Wever

Auteur	Xiaomei Yan
Auteur	Rienk Nieuwland
Auteur	Marca H. M. Wauben
Auteur	John P. Nolan
Auteur	Jennifer C. Jones
Résumé	Extracellular vesicles (EVs) are small, heterogeneous and difficult to measure. Flow cytometry (FC) is a key technology for the measurement of individual particles, but its application to the analysis of EVs and other submicron particles has presented many challenges and has produced a number of controversial results, in part due to limitations of instrument detection, lack of robust methods and ambiguities in how data should be interpreted. These complications are exacerbated by the field's lack of a robust reporting framework, and many EV-FC manuscripts include incomplete descriptions of methods and results, contain artefacts stemming from an insufficient instrument sensitivity and inappropriate experimental design and lack appropriate calibration and standardization. To address these issues, a working group (WG) of EV-FC researchers from ISEV, ISAC and ISTH, worked together as an EV-FC WG and developed a consensus framework for the minimum information that should be provided regarding EV-FC. This framework incorporates the existing Minimum Information for Studies of EVs (MISEV) guidelines and Minimum Information about a FC experiment (MIFlowCyt) standard in an EV-FC-specific reporting framework (MIFlowCyt-EV) that supports reporting of critical information related to sample staining, EV detection and measurement and experimental design in manuscripts that report EV-FC data. MIFlowCyt-EV provides a structure for sharing EV-FC results, but it does not prescribe specific protocols, as there will continue to be rapid evolution of instruments and methods for the foreseeable future. MIFlowCyt-EV accommodates this evolution, while providing information needed to evaluate and compare different approaches. Because MIFlowCyt-EV will ensure consistency in the manner of reporting of EV-FC studies, over time we expect that adoption of MIFlowCyt-EV as a standard for reporting EV-FC studies will improve the ability to quantitatively compare results from different laboratories and to support the development of new instruments and assays for improved measurement of EVs.
Date	2020
Langue	eng
Titre abrégé	MIFlowCyt-EV
Catalogue de bibl.	PubMed
Extra	Number: 1
Volume	9
Pages	1713526
Publication	Journal of Extracellular Vesicles
DOI	10.1080/20013078.2020.1713526

Numéro	1
Abrév. de revue	J Extracell Vesicles
ISSN	2001-3078
Date d'ajout	13/12/2021 10:36:14
Modifié le	13/12/2021 10:36:14

- **Marqueurs :**
  - extracellular vesicles
  - Flow Cytometry
  - standardization
  - framework
  - reporting

  Pièces jointes

  - PubMed entry
  - Texte intégral

- ## Neutrophil extracellular traps are associated with the pathogenesis of diffuse alveolar hemorrhage in murine lupus

Type de document	Article de revue
Auteur	Pierre-André Jarrot
Auteur	Edwige Tellier
Auteur	Lea Plantureux
Auteur	Lydie Crescence
Auteur	Stéphane Robert
Auteur	Corinne Chareyre
Auteur	Laurent Daniel
Auteur	Véronique Secq
Auteur	Stéphane Garcia
Auteur	Françoise Dignat-George
Auteur	Laurence Panicot-Dubois
Auteur	Christophe Dubois
Auteur	Gilles Kaplanski
Résumé	Diffuse alveolar hemorrhage (DAH) is a life-threatening complication of systemic lupus erythematosus (SLE) and systemic vasculitis. Although initially described to have antibacterial properties, increasing evidence suggests that neutrophil extracellular traps (NETs) have a detrimental role in both autoimmune diseases and acute lung injury. We investigated whether NETs could be detected in a murine model of

pristane-induced lupus DAH and contribute to lung injury. Such NETs might constitute a therapeutic target. NETs were characterized by immunofluorescence staining of DNA, neutrophil elastase and citrullinated histones. Evaluation of lung injury was performed by haematoxylin-eosin staining and a quantification program. Clinical status of the mice was assessed by measurement of arterial oxygen saturation and survival curves after recombinant human deoxyribonuclease-1 (Rh-DNase-1) inhalations or polymorphonuclear neutrophil (PMN) depletion. Pristane was found to promote NETs formation in vitro and in vivo. Treatment of mice with Rh-DNase-1 inhalations cleared NETs and reduced lung injury. Clinical status improved significantly, with increased arterial oxygenation and survival. Following PMN depletion, NETs were absent with a subsequent reduction of lung injury and improved arterial oxygenation. These results support a pathogenic role of PMNs and NETs in lung injury during pristane-induced DAH. Targeting NETs with Rh-DNase-1 inhalations could constitute an interesting adjuvant therapy in human DAH.

Date	Jun 2019
Langue	eng
Catalogue de bibl.	PubMed
Volume	100
Pages	120-130
Publication	Journal of Autoimmunity
DOI	10.1016/j.jaut.2019.03.009
Abrév. de revue	J. Autoimmun.
ISSN	1095-9157
Date d'ajout	13/12/2021 10:34:50
Modifié le	13/12/2021 10:34:50

- **Marqueurs :**
  - Neutrophil extracellular traps
  - Deoxyribonuclease-1
  - Diffuse alveolar hemorrhage
  - Murine model
  - Systemic lupus erythematosus

Pièces jointes

  - PubMed entry

- ## Extracellular vesicles from T cells overexpress miR-146b-5p in HIV-1 infection and repress endothelial activation

Type de document	Article de revue
Auteur	Estelle Balducci
Auteur	Aurélie S. Leroyer
Auteur	Romaric Lacroix
Auteur	Stéphane Robert
Auteur	Dilyana Todorova
Auteur	Stéphanie Simoncini
Auteur	Luc Lyonnet
Auteur	Corinne Chareyre
Auteur	Olivia Zaegel-Faucher
Auteur	Joëlle Micallef
Auteur	Isabelle Poizot-Martin
Auteur	Patrice Roll
Auteur	Françoise Dignat-George
Résumé	Human immunodeficiency virus type 1 (HIV-1) infection promotes a generalized activation of host responses that involves not only CD4 T cells, but also cells of the microenvironment, which are not directly infected, such as endothelial cells. The mechanisms triggering HIV-1-associated vascular alterations remain poorly understood. Extracellular vesicles (EVs), implicated in cell-to-cell communication, have been recently described as carriers of microRNAs (miRNAs). Here, we show that miR-146b-5p is upregulated in both CD4 T cells, CD4 T cell-derived EVs and circulating EVs obtained from antiretroviral therapy-naive HIV-1-infected patients. We further demonstrate that EVs from T cell line overexpressing miR-146b-5p mimics (miR-146b-EVs): 1) protect their miRNA cargo from RNase degradation, 2) transfer miR-146b-5p mimics into endothelial cells and 3) reduce endothelial inflammatory responses in vitro and in vivo in the lungs of mice through the downregulation of nuclear factor-κB-responsive molecules. These data advance our understanding on chronic inflammatory responses affecting endothelial homeostasis, in infectious and non-infectious diseases and pave the way for potential new anti-inflammatory strategies.
Date	07 16, 2019
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 1
Volume	9
Pages	10299
Publication	Scientific Reports
DOI	10.1038/s41598-019-44743-w
Numéro	1

Abrév. de revue	Sci Rep
ISSN	2045-2322
Date d'ajout	13/12/2021 10:34:50
Modifié le	13/12/2021 10:34:50

- **Pièces jointes**
  - PubMed entry
  - Texte intégral
- # CD146 deficiency promotes plaque formation in a mouse model of atherosclerosis by enhancing RANTES secretion and leukocyte recruitment

Type de document	Article de revue
Auteur	Muriel G. Blin
Auteur	Richard Bachelier
Auteur	Karim Fallague
Auteur	Karima Moussouni
Auteur	Michel Aurrand-Lions
Auteur	Samantha Fernandez
Auteur	Benjamin Guillet
Auteur	Stéphane Robert
Auteur	Alexandrine Foucault-Bertaud
Auteur	Nathalie Bardin
Auteur	Marcel Blot-Chabaud
Auteur	Françoise Dignat-George
Auteur	Aurélie S. Leroyer
Résumé	AIMS: The progression of atherosclerosis is based on the continued recruitment of leukocytes in the vessel wall. The previously described role of CD146 in leukocyte infiltration suggests an involvement for this adhesion molecule in the inflammatory response. In this study, we investigated the role of CD146 in leukocyte recruitment by using an experimental model of atherogenesis. METHODS AND RESULTS: The role of CD146 was explored in atherosclerosis by crossing CD146-/- mice with ApoE-/- mice. CD146 -/-/ApoE -/- and ApoE -/- mice were fed a Western diet for 24 weeks and were monitored for aortic wall thickness using high frequency ultrasound. The arterial wall was significantly thicker in CD146-deficient mice. After 24 weeks of Western diet, a significant increase of atheroma in both total aortic lesion and aortic sinus of CD146-null mice was observed. In addition, atherosclerotic lesions were more inflammatory since plaques from CD146-deficient mice contained more neutrophils and macrophages. This was due to up-regulation of RANTES secretion by macrophages in

CD146-deficient atherosclerotic arteries. This prompted us to further address the function of CD146 in leukocyte recruitment during acute inflammation by using a second experimental model of peritonitis induced by thioglycollate. Neutrophil recruitment was significantly increased in CD146-deficient mice 12 h after peritonitis induction and associated with higher RANTES levels in the peritoneal cavity. In CD146-null macrophages, we also showed that increased RANTES production was dependent on constitutive inhibition of the p38-MAPK signaling pathway. Finally, Maraviroc, a RANTES receptor antagonist, was able to reduce atherosclerotic lesions and neutrophilia in CD146-deficient mice to the same level as that found in ApoE -/- mice. CONCLUSIONS: Our data indicate that CD146 deficiency is associated with the upregulation of RANTES production and increased inflammation of atheroma, which could influence the atherosclerotic plaque fate. Thus, these data identify CD146 agonists as potential new therapeutic candidates for atherosclerosis treatment.

Date	05 2019
Langue	eng
Catalogue de bibl.	PubMed
Volume	130
Pages	76-87
Publication	Journal of Molecular and Cellular Cardiology
DOI	10.1016/j.yjmcc.2019.03.017
Abrév. de revue	J. Mol. Cell. Cardiol.
ISSN	1095-8584
Date d'ajout	13/12/2021 10:35:04
Modifié le	13/12/2021 10:35:04

- **Pièces jointes**
  - PubMed entry
  - Version soumise

- # Natural Killer Cells Exhibit a Peculiar Phenotypic Profile in Systemic Sclerosis and Are Potent Inducers of Endothelial Microparticles Release

Type de document	Article de revue
Auteur	Audrey Benyamine
Auteur	Jérémy Magalon
Auteur	Florence Sabatier
Auteur	Luc Lyonnet
Auteur	Stéphane Robert

Auteur	Chloé Dumoulin
Auteur	Sophie Morange
Auteur	Karin Mazodier
Auteur	Gilles Kaplanski
Auteur	Martine Reynaud-Gaubert
Auteur	Pascal Rossi
Auteur	Françoise Dignat-George
Auteur	Brigitte Granel
Auteur	Pascale Paul
Résumé	The pathophysiology of systemic sclerosis (SSc) involves early endothelial and immune activation, both preceding the onset of fibrosis. We previously identified soluble fractalkine and circulating endothelial microparticles (EMPs) as biomarkers of endothelial inflammatory activation in SSc. Fractalkine plays a dual role as a membrane-bound adhesion molecule expressed in inflamed endothelial cells (ECs) and as a chemokine involved in the recruitment, transmigration, and cytotoxic activation of immune cells that express CX3CR1, the receptor of fractalkine, namely CD8 and γδ T cells and natural killer (NK) cells. We aimed to quantify circulating cytotoxic immune cells and their expression of CX3CR1. We further investigated the expression profile of NK cells chemokine receptors and activation markers and the potential of NK cells to induce EC activation in SSc. We performed a monocentric study (NCT 02636127) enrolling 15 SSc patients [15 females, median age of 55 years (39-63), 11 limited cutaneous form and 4 diffuse] and 15 healthy controls. Serum fractalkine levels were significantly increased in SSc patients. Circulating CD8 T cells numbers were decreased in SSc patients with no difference in their CX3CR1 expression. Circulating γδ T cells and NK cells numbers were preserved. CX3CR1 expression in CD8 and γδ T cells did not differ between SSc patients and controls. The percentage and level of CX3CR1 expression in NK cells were significantly lowered in SSc patients. Percentages of CXCR4, NKG2D, CD69-expressing NK cells, and their expression levels were decreased in NK cells. Conversely, CD16 level expression and percentages of CD16+ NK cells were preserved. The exposure of human microvascular dermic EC line (HMVEC-d) to peripheral blood mononuclear cells resulted in similar NK cells degranulation activity in SSc patients and controls. We further showed that NK cells purified from the blood of SSc patients induced enhanced release of EMPs than NK cells from controls. This study evidenced a peculiar NK cells phenotype in SSc characterized by decreased chemokine and activation receptors expression, that might reflect NK cells involvement in the pathogenic process. It also highlighted the role of NK cells as a potent mechanism inducing endothelial activation through enhanced EMPs release.
Date	2018
Langue	eng

Catalogue de bibl.	PubMed
Volume	9
Pages	1665
Publication	Frontiers in Immunology
DOI	10.3389/fimmu.2018.01665
Abrév. de revue	Front Immunol
ISSN	1664-3224
Date d'ajout	13/12/2021 10:35:05
Modifié le	13/12/2021 10:35:05

- **Marqueurs :**
    - CX3CR1
    - endothelial microparticles
    - fractalkine
    - natural killer cells
    - systemic sclerosis

  Pièces jointes

    - PubMed entry
    - Texte intégral

- # A new assay to evaluate microvesicle plasmin generation capacity: validation in disease with fibrinolysis imbalance

Type de document	Article de revue
Auteur	Sylvie Cointe
Auteur	Karim Harti Souab
Auteur	Tarik Bouriche
Auteur	Loris Vallier
Auteur	Amandine Bonifay
Auteur	Coralie Judicone
Auteur	Stéphane Robert
Auteur	Romain Armand
Auteur	Philippe Poncelet
Auteur	Jacques Albanese
Auteur	Françoise Dignat-George
Auteur	Romaric Lacroix
Résumé	Among extracellular vesicles, leukocyte-derived microvesicles (LMVs) have emerged as complex vesicular structures. Primarily identified as

procoagulant entities, they were more recently ascribed to plasmin generation capacity (MV-PGC). The objectives of this work were (1) to develop a new hybrid bio-assay combining the specific isolation of LMVs and measurement of their PGC, and compare its performance to the original method based on centrifugation, (2) to validate MV-PGC in septic shock, combining increased levels of LMVs and fibrinolytic imbalance. Using plasma sample spiked with LMVs featuring different levels of PGC, we demonstrated that CD15-beads specifically extracted LMVs. The MV dependency of the test was demonstrated using electron microscopy, high speed centrifugation, nanofiltration and detergent-mediated solubilization and the MV-PGC specificity using plasmin-specific inhibitors, or antibodies blocking elastase or uPA. Thanks to a reaction booster (ε-ACA), we showed that the assay was more sensitive and reproducible than the original method. Moreover, it exhibited a good repeatability, inter-operator and inter-experiment reproducibility. The new immunomagnetic bio-assay was further validated in patients with septic shock. As a result, we showed that MV-PGC values were significantly lower in septic shock patients who died compared to patients who survived, both at inclusion and 24 h later (1.4 [0.8-3.0] vs 3.1 [1.7-18] A405 × 10-3/min, p = 0.02; 1.4 [1-1.6] vs 5.2 [2.2-16] A405 × 10-3/min, p = 0.004). Interestingly, combining both MV-PGC and PAI-1 in a ratio significantly improved the predictive value of PAI-1. This strategy, a hybrid capture bioassay to specifically measure LMV-PGC using for the first time, opens new perspectives for measuring subcellular fibrinolytic potential in clinical settings with fibrinolytic imbalance.

Date	2018
Langue	eng
Titre abrégé	A new assay to evaluate microvesicle plasmin generation capacity
Catalogue de bibl.	PubMed
Extra	Number: 1
Volume	7
Pages	1494482
Publication	Journal of Extracellular Vesicles
DOI	10.1080/20013078.2018.1494482
Numéro	1
Abrév. de revue	J Extracell Vesicles
ISSN	2001-3078
Date d'ajout	13/12/2021 10:35:05
Modifié le	13/12/2021 10:35:05

- ## Marqueurs :
  - extracellular vesicles

- Fibrinolysis
- Microvesicles
- immunomagnetic separation
- septic shock

Pièces jointes

- PubMed entry
- Texte intégral

- ## A novel anti-CD146 antibody specifically targets cancer cells by internalizing the molecule

Type de document	Article de revue
Auteur	Marie Nollet
Auteur	Jimmy Stalin
Auteur	Anaïs Moyon
Auteur	Waël Traboulsi
Auteur	Amel Essaadi
Auteur	Stéphane Robert
Auteur	Nausicaa Malissen
Auteur	Richard Bachelier
Auteur	Laurent Daniel
Auteur	Alexandrine Foucault-Bertaud
Auteur	Caroline Gaudy-Marqueste
Auteur	Romaric Lacroix
Auteur	Aurélie S. Leroyer
Auteur	Benjamin Guillet
Auteur	Nathalie Bardin
Auteur	Françoise Dignat-George
Auteur	Marcel Blot-Chabaud
Résumé	CD146 is an adhesion molecule present on many tumors (melanoma, kidney, pancreas, breast, ...). In addition, it has been shown to be expressed on vascular endothelial and smooth muscle cells. Generating an antibody able to specifically recognize CD146 in cancer cells (designated as tumor CD146), but not in normal cells, would thus be of major interest for targeting tumor CD146 without affecting the vascular system. We thus generated antibodies against the extracellular domain of the molecule produced in cancer cells and selected an antibody that specifically recognizes tumor CD146. This antibody (TsCD146 mAb) was able to detect CD146-positive tumors in human biopsies and in vivo, by PET imaging, in a murine xenograft model. In addition, TsCD146 mAb antibody was able to specifically detect CD146-positive cancer microparticles in the plasma of patients. TsCD146 mAb displayed also therapeutic effects since it was able to reduce the growth

of human CD146-positive cancer cells xenografted in nude mice. This effect was due to a decrease in the proliferation and an increase in the apoptosis of CD146-positive cancer cells after TsCD146-mediated internalization of the cell surface CD146. Thus, TsCD146 mAb could be of major interest for diagnostic and therapeutic strategies against CD146-positive tumors in a context of personalized medicine.

Date	Dec 22, 2017
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 68
Volume	8
Pages	112283-112296
Publication	Oncotarget
DOI	10.18632/oncotarget.22736
Numéro	68
Abrév. de revue	Oncotarget
ISSN	1949-2553
Date d'ajout	13/12/2021 10:35:05
Modifié le	13/12/2021 10:35:05

- **Marqueurs :**
    - antibody
    - cancer
    - CD146
    - PET
    - therapy

  Pièces jointes

    - PubMed entry
    - Texte intégral

- ## Standardization of microparticle enumeration across different flow cytometry platforms: results of a multicenter collaborative workshop

Type de document	Article de revue
Auteur	S. Cointe
Auteur	C. Judicone
Auteur	S. Robert
Auteur	M.J. Mooberry
Auteur	P. Poncelet

Auteur	M. Wauben
Auteur	R. Nieuwland
Auteur	N. S. Key
Auteur	F. Dignat-George
Auteur	R. Lacroix
Résumé	Background Microparticles are extracellular vesicles resulting from the budding of cellular membranes that have a high potential as emergent biomarkers; however, their clinical relevance is hampered by methodological enumeration concerns and a lack of standardization. Flow cytometry (FCM) remains the most commonly used technique with the best capability to determine the cellular origin of single MPs. However, instruments behave variably depending on which scatter parameter, (Forward (FSC) or Side scatter (SSC)), provides the best resolution to discriminate submicron particles. To overcome this problem, a new approach, based on two sets of selected beads adapted to FSC or SSC optimized instruments, was recently proposed to reproducibly enumerate platelet-derived MP counts among instruments with different optical systems. Objective The objective was to evaluate this strategy in an international workshop that included 44 laboratories accounting for 52 cytometers of 14 types. Methods/Results Using resolution capability and background noise level as criteria to qualify the instruments, the standardization strategy proved to be compatible with 85% (44/52) instruments. All instruments correctly ranked the PMP levels of two platelet-free plasma samples. The inter-laboratory variability of PMP counts was 37% and 28% for each sample. No difference was found between instruments using forward or side scattered light as the relative sizing parameter. Conclusions Despite remaining limitations, this study is the first to demonstrate a real potential of bead-based strategies for standardization of MP enumeration across different FCM platforms. Additional standardization efforts are still mandatory to evaluate MP clinical relevance at a multicenter level.
Date	2017-1
Titre abrégé	Standardization of microparticle enumeration across different flow cytometry platforms
Catalogue de bibl.	PubMed Central
URL	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5280151/
Consulté le	27/09/2023 15:32:56
Extra	PMID: 27662257 PMCID: PMC5280151
Volume	15
Pages	187-193
Publication	Journal of thrombosis and haemostasis : JTH
DOI	10.1111/jth.13514
Numéro	1

Abrév. de revue	J Thromb Haemost
ISSN	1538-7933
Date d'ajout	27/09/2023 15:32:56
Modifié le	27/09/2023 15:32:56

- **Pièces jointes**
  - Full Text PDF
  - PubMed Central Link
- # Biogenesis of Pro-senescent Microparticles by Endothelial Colony Forming Cells from Premature Neonates is driven by SIRT1-Dependent Epigenetic Regulation of MKK6

Type de document	Article de revue
Auteur	Stéphanie Simoncini
Auteur	Anne-Line Chateau
Auteur	Stéphane Robert
Auteur	Dilyana Todorova
Auteur	Catherine Yzydorzick
Auteur	Romaric Lacroix
Auteur	Isabelle Ligi
Auteur	Laurence Louis
Auteur	Richard Bachelier
Auteur	Umberto Simeoni
Auteur	Frédérique Magdinier
Auteur	Françoise Dignat-George
Auteur	Florence Sabatier
Résumé	Senescent cells may exert detrimental effect on microenvironment through the secretion of soluble factors and the release of extracellular vesicles, such as microparticles, key actors in ageing and cardiovascular diseases. We previously reported that sirtuin-1 (SIRT1) deficiency drives accelerated senescence and dysfunction of endothelial colony-forming cells (ECFC) in PT neonates. Because preterm birth (PT) increases the risk for cardiovascular diseases during neonatal period as well as at adulthood, we hypothesized that SIRT1 deficiency could control the biogenesis of microparticles as part of a senescence-associated secretory phenotype (SASP) of PT-ECFC and investigated the related molecular mechanisms. Compared to control ECFC, PT-ECFC displayed a SASP associated with increased release of endothelial microparticles (EMP), mediating a paracrine induction of senescence in naïve endothelial cells. SIRT1 level inversely correlated

with EMP release and drives PT-ECFC vesiculation. Global transcriptomic analysis revealed changes in stress response pathways, specifically the MAPK pathway. We delineate a new epigenetic mechanism by which SIRT1 deficiency regulates MKK6/p38MAPK/Hsp27 pathway to promote EMP biogenesis in senescent ECFC. These findings deepen our understanding of the role of ECFC senescence in the disruption of endothelial homeostasis and provide potential new targets towards the control of cardiovascular risk in individuals born preterm.

Date	08 15, 2017
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 1
Volume	7
Pages	8277
Publication	Scientific Reports
DOI	[10.1038/s41598-017-08883-1](https://doi.org/10.1038/s41598-017-08883-1)
Numéro	1
Abrév. de revue	Sci Rep
ISSN	2045-2322
Date d'ajout	13/12/2021 10:35:05
Modifié le	13/12/2021 10:35:05

- ## Marqueurs :
  - Humans
  - Models, Biological
  - Cell-Derived Microparticles
  - Endothelial Cells
  - Signal Transduction
  - Cellular Senescence
  - Gene Expression Profiling
  - Transcriptome
  - Gene Expression Regulation
  - Endothelial Progenitor Cells
  - Epigenesis, Genetic
  - Gene Deletion
  - Infant, Newborn
  - MAP Kinase Kinase 6
  - p38 Mitogen-Activated Protein Kinases
  - Paracrine Communication
  - Premature Birth
  - Sirtuin 1

Pièces jointes

- PubMed entry
- Texte intégral

- **Standardization of microparticle enumeration across different flow cytometry platforms: results of a multicenter collaborative workshop**

Type de document	Article de revue
Auteur	S. Cointe
Auteur	C. Judicone
Auteur	S. Robert
Auteur	M. J. Mooberry
Auteur	P. Poncelet
Auteur	M. Wauben
Auteur	R. Nieuwland
Auteur	N. S. Key
Auteur	F. Dignat-George
Auteur	R. Lacroix
Résumé	Essentials The clinical enumeration of microparticles (MPs) is hampered by a lack of standardization. A new strategy to standardize MP counts by flow cytometry was evaluated in a multicenter study. No difference was found between instruments using forward or side scatter as the trigger parameter. This study demonstrated that beads can be used as a standardization tool for MPs. Click to hear the ISTH Academy's webinar on microvesicles SUMMARY: Background Microparticles (MPs) are extracellular vesicles resulting from the budding of cellular membranes that have a high potential as emergent biomarkers; however, their clinical relevance is hampered by methodological enumeration concerns and a lack of standardization. Flow cytometry (FCM) remains the most commonly used technique with the best capability to determine the cellular origin of single MPs. However, instruments behave variably depending on which scatter parameter (forward (FSC) or side scatter (SSC)) provides the best resolution to discriminate submicron particles. To overcome this problem, a new approach, based on two sets of selected beads adapted to FSC or SSC-optimized instruments, was recently proposed to reproducibly enumerate platelet-derived MP counts among instruments with different optical systems. Objective The objective was to evaluate this strategy in an international workshop that included 44 laboratories accounting for 52 cytometers of 14 types. Methods/Results Using resolution capability and background noise level as criteria to qualify the instruments, the standardization strategy proved to be compatible with 85% (44/52) of instruments. All instruments correctly ranked the platelet MP (PMP) levels of two platelet-free plasma samples. The inter-laboratory variability of PMP counts was 37% and 28% for each sample. No difference was found between instruments using forward or

side-scattered light as the relative sizing parameter. Conclusions Despite remaining limitations, this study is the first to demonstrate a real potential of bead-based strategies for standardization of MP enumeration across different FCM platforms. Additional standardization efforts are still mandatory to evaluate MPs' clinical relevance at a multicenter level.

Date	01 2017
Langue	eng
Titre abrégé	Standardization of microparticle enumeration across different flow cytometry platforms
Catalogue de bibl.	PubMed
Extra	Number: 1
Volume	15
Pages	187-193
Publication	Journal of thrombosis and haemostasis: JTH
DOI	[10.1111/jth.13514](https://doi.org/10.1111/jth.13514)
Numéro	1
Abrév. de revue	J. Thromb. Haemost.
ISSN	1538-7836
Date d'ajout	13/12/2021 10:35:06
Modifié le	13/12/2021 10:35:06

- **Marqueurs :**
  - extracellular vesicles
  - plasma
  - Humans
  - Particle Size
  - Cell-Derived Microparticles
  - Flow Cytometry
  - Neutrophils
  - Calibration
  - Sensitivity and Specificity
  - multicenter study
  - Platelet Count
  - standardization

  Pièces jointes

  - PubMed entry
  - Version acceptée

- # Soluble CD146, an innovative and non-invasive biomarker of embryo selection for in vitro fertilization

Type de document	Article de revue
Auteur	Sylvie Bouvier
Auteur	Odile Paulmyer-Lacroix
Auteur	Nicolas Molinari
Auteur	Alexandrine Bertaud
Auteur	Marine Paci
Auteur	Aurélie Leroyer
Auteur	Stéphane Robert
Auteur	Françoise Dignat George
Auteur	Marcel Blot-Chabaud
Auteur	Nathalie Bardin
Résumé	Although progress was made in in vitro fertilization (IVF) techniques, the majority of embryos transferred fail to implant. Morphology embryo scoring is the standard procedure for most of IVF centres for choosing the best embryo, but remains limited since even the embryos classified as "top quality" may not implant. As it has been shown that i) CD146 is involved in embryo implantation and ii) membrane form is shed to generate soluble CD146 (sCD146), we propose that sCD146 in embryo supernatants may constitute a new biomarker of embryo selection. Immunocytochemical staining showed expression of CD146 in early embryo stages and sCD146 was detected by ELISA and Western-blot in embryo supernatants from D2. We retrospectively studied 126 couples who underwent IVF attempt. The embryo culture medium from each transferred embryo (n = 222) was collected for measurement of sCD146 by ELISA. Significantly higher sCD146 concentrations were present in embryo supernatants that did not implant (n = 185) as compared to those that successfully implanted (n = 37) (1310 +/- 1152 pg.mL-1 vs. 845+/- 1173 pg.mL-1, p = 0.024). Sensitivity analysis performed on single embryo transfers (n = 71) confirmed this association (p = 0.0054). The computed ROC curve established that the optimal sCD146 concentration for embryo implantation is under 1164 pg.mL-1 (sensitivity: 76%, specificity: 48%, PPV: 25% and NPV: 92%). Over this sCD146 threshold, the implantation rate was significantly lower (9% with sCD146 levels >1164 pg.ml-1 vs. 22% with sCD146 levels ≤ 1164 pg.mL-1, p = 0.01). Among the embryos preselected by morphologic scoring, sCD146 determination could allow a better selection of the embryo(s), thus improving the success of elective single embryo transfer. This study establishes the proof of concept for the use of sCD146 as a biomarker for IVF by excluding the embryo with the highest sCD146 level. A multicentre prospective study will now be necessary to further establish its use in clinical practice.
Date	2017
Langue	eng
Catalogue de bibl.	PubMed

Extra	Number: 3
Volume	12
Pages	e0173724
Publication	PloS One
DOI	10.1371/journal.pone.0173724
Numéro	3
Abrév. de revue	PLoS ONE
ISSN	1932-6203
Date d'ajout	13/12/2021 10:35:06
Modifié le	13/12/2021 10:35:06

- **Marqueurs :**
  - Humans
  - Adult
  - Biomarkers
  - Female
  - CD146 Antigen
  - Embryo Implantation
  - Fertilization in Vitro

  Pièces jointes

  - PubMed entry
  - Texte intégral

- ## The origin and concentration of circulating microparticles differ according to cancer type and evolution: A prospective single-center study

Type de document	Article de revue
Auteur	Diane Mege
Auteur	Laurence Panicot-Dubois
Auteur	Mehdi Ouaissi
Auteur	Stéphane Robert
Auteur	Igor Sielezneff
Auteur	Bernard Sastre
Auteur	Françoise Dignat-George
Auteur	Christophe Dubois
Résumé	Microparticles are plasma membrane vesicles produced by apoptotic or activated cells and resting cancer cells. The concentration, origin and procoagulant properties of circulating microparticles are reported to differ according to pathological settings (inflammation, cancer and cardiovascular diseases). In case of cancer, different studies have

reported a variation in the concentration of circulating microparticles, with an increase in procoagulant and tumor-associated antigen-bearing microparticles. However, the cancer specificity of these results remains unknown. The objective was to establish a specific signature of colorectal and pancreatic cancers (CRC, PC) by characterizing circulating microparticles. Patients presenting with CRC, PC, inflammatory bowel or pancreatic diseases, and healthy subjects, were prospectively included. Circulating microparticles were analyzed by flow cytometry, combining the analysis of Annexin V-positive with characterization of their origin and determination of their procoagulant activities. We included 85, 36, 15, 18 and 20 patients presenting with CRC, PC, inflammatory bowel or pancreatic diseases, and healthy subjects, respectively. Here, we depict a specific signature, which differed between CRC, PC, associated inflammatory bowel and pancreatic diseases and healthy subjects. Furthermore, in patients with remission, this signature returned to the levels observed in associated inflammatory or healthy patients. Our results indicate that circulating microparticles differ depending on the evolution of a cancer. The analysis of the circulating microparticles reveals the specificity of the signature and can be used as a new complex biomarker reflecting the evolution of the disease.

Date	Feb 15, 2016
Langue	eng
Titre abrégé	The origin and concentration of circulating microparticles differ according to cancer type and evolution
Catalogue de bibl.	PubMed
Extra	Number: 4
Volume	138
Pages	939-948
Publication	International Journal of Cancer
DOI	10.1002/ijc.29837
Numéro	4
Abrév. de revue	Int. J. Cancer
ISSN	1097-0215
Date d'ajout	13/12/2021 10:35:06
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- **Marqueurs :**
  - Humans
  - Cell-Derived Microparticles
  - Flow Cytometry
  - Adult
  - Female
  - Male
  - Aged

- Middle Aged
- microparticle
- Aged, 80 and over
- Biomarkers, Tumor
- Prospective Studies
- Colorectal Neoplasms
- Colitis
- colorectal cancer
- microparticulosome
- pancreatic cancer
- Pancreatic Neoplasms
- Pancreatitis, Chronic

Pièces jointes

- PubMed entry
- Texte intégral

- ## Standardized counting of circulating platelet microparticles using currently available flow cytometers and scatter-based triggering: Forward or side scatter?

Type de document	Article de revue
Auteur	P. Poncelet
Auteur	S. Robert
Auteur	T. Bouriche
Auteur	J. Bez
Auteur	R. Lacroix
Auteur	F. Dignat-George
Résumé	Clinical determination of MP counts using flow cytometry has not been fully accepted yet due to the lack of standardization protocols. In the past 5 years, we have proposed two versions of a method with reproducible PMP counts in plasma samples. Both methods use forward scatter (FSC)-based threshold set with reference beads of appropriate sizes; first using 0.5 µm beads and later with 0.3 µm beads. Both systems provide reproducible PMP counts. However, this technique works only with some of currently used commercial flow cytometers. Instruments with limited resolution or generating heterogeneous FSC signals are excluded. Such performances are incompatible with the required interinstrument standardization. Here we show that (i) flow cytometers with sub-optimal FSC capabilities generally have higher SSC resolution and background rejection capacity, and (ii) that the same biological entities, "dim and bright PMP," both can be counted using alternative strategies, either as previously described, based on FSC measurements, or as presented

here, based on SSC detection. The critical element in the standardization protocol is the use of different sizes of reference beads. This study was designed to permit simultaneous access to both FSC- and SSC-optimized platforms. A new range of about 0.17-0.6 µm eq. (µm-equivalents) is proposed for an alternative SSC-based MP gate generating the same PMP counts as those obtained in the previously proposed 0.3-1 µm eq. FSC-based MP gate. The two equivalent standardization options reconcile intrinsically different scattering behaviors between SSC- and FCS--triggered instruments and open the opportunity for multicenter studies in the future.

Date	Feb 2016
Langue	eng
Titre abrégé	Standardized counting of circulating platelet microparticles using currently available flow cytometers and scatter-based triggering
Catalogue de bibl.	PubMed
Extra	Number: 2
Volume	89
Pages	148-158
Publication	Cytometry. Part A: The Journal of the International Society for Analytical Cytology
DOI	10.1002/cyto.a.22685
Numéro	2
Abrév. de revue	Cytometry A
ISSN	1552-4930
Date d'ajout	13/12/2021 10:35:20
Modifié le	13/12/2021 10:35:20

- **Marqueurs :**
  - Blood Platelets
  - Humans
  - Cell-Derived Microparticles
  - Flow Cytometry
  - reference standards
  - microparticles
  - Microvesicles
  - Platelet Count
  - standardization
  - absolute counting
  - extra-cellular vesicles
  - interplatform reproducibility
  - Light
  - scatter
  - Scattering, Radiation
  - submicron particles

Pièces jointes

- Poncelet et al. - 2016 - Standardized counting of circulating platelet micr.pdf
- PubMed entry

- ## Detection of EpCAM-positive microparticles in pleural fluid: A new approach to mini-invasively identify patients with malignant pleural effusions

Type de document	Article de revue
Auteur	Elisa Roca
Auteur	Romaric Lacroix
Auteur	Coralie Judicone
Auteur	Sophie Laroumagne
Auteur	Stéphane Robert
Auteur	Sylvie Cointe
Auteur	Alexandre Muller
Auteur	Elise Kaspi
Auteur	Patrice Roll
Auteur	Alain R. Brisson
Auteur	Claudio Tantucci
Auteur	Philippe Astoul
Auteur	Françoise Dignat-George
Résumé	Pleural biomarkers allowing to mini-invasively discriminate benign from malignant pleural effusions are needed. Among potential candidates, microparticles (MPs) are extracellular vesicles that vectorize antigen derived from the parent cell. We hypothesized that tumor-derived MPs could be present in the pleural liquid and help to identify patients with malignant pleural effusions. Using highly sensitive flow cytometry and cryo-electron microscopy, we showed that large amounts of MPs from hematopoïetic and vascular origin could be detectable in pleural fluids. Their level did not differ between benign (n = 14) and malignant (n = 71) pleural effusions. Analysis of selected tumoral associated antigens (podoplanin, mucin 1 and EpCAM, epithelial-cell-adhesion-molecule) evidenced for the first time the presence of tumor-derived MPs expressing EpCAM in malignant pleural fluids only (Specificity = 93%, Sensitivity = 49% and 45% for flow cytometry and ELISA, respectively). The detection of EpCAM-positive-MPs (EpCAM + MPs) by flow cytometry showed a better specificity and sensitivity than ELISA to distinguish between pleural carcinoma and the others malignant pleural effusions (MPE; Sp: 96% vs 89%; Se: 79% vs 66%). Combining EpCAM+ MPs and cytology improved the diagnosis of MPE compared to cytology alone. This study establishes the basis for using EpCAM+ MPs as a promising new

biomarker that could be added to the armamentarium to mini-invasively identify patients with malignant pleural effusions.

Date	Jan 19, 2016
Langue	eng
Titre abrégé	Detection of EpCAM-positive microparticles in pleural fluid
Catalogue de bibl.	PubMed
Extra	Number: 3
Volume	7
Pages	3357-3366
Publication	Oncotarget
DOI	10.18632/oncotarget.6581
Numéro	3
Abrév. de revue	Oncotarget
ISSN	1949-2553
Date d'ajout	13/12/2021 10:35:06
Modifié le	13/12/2021 10:35:06

- ## Marqueurs :
    - extracellular vesicles
    - Humans
    - Cell-Derived Microparticles
    - Flow Cytometry
    - Female
    - Male
    - Enzyme-Linked Immunosorbent Assay
    - Microscopy, Electron, Transmission
    - Neoplasms
    - Biomarkers, Tumor
    - Cryoelectron Microscopy
    - EpCAM
    - Epithelial Cell Adhesion Molecule
    - microparticles
    - pleural effusion
    - Pleural Effusion, Malignant
    - pleural neoplasia
    - Prospective Studies

Pièces jointes

- PubMed entry
- Texte intégral

- ## Platelet and not erythrocyte microparticles are procoagulant in transfused thalassaemia major patients

Type de document	Article de revue
Auteur	Imane Agouti
Auteur	Sylvie Cointe
Auteur	Stéphane Robert
Auteur	Coralie Judicone
Auteur	Anderson Loundou
Auteur	Fathi Driss
Auteur	Alain Brisson
Auteur	Dominique Steschenko
Auteur	Christian Rose
Auteur	Corinne Pondarré
Auteur	Emmanuelle Bernit
Auteur	Catherine Badens
Auteur	Françoise Dignat-George
Auteur	Romaric Lacroix
Auteur	Isabelle Thuret
Résumé	The level of circulating platelet-, erythrocyte-, leucocyte- and endothelial-derived microparticles detected by high-sensitivity flow cytometry was investigated in 37 β-thalassaemia major patients receiving a regular transfusion regimen. The phospholipid procoagulant potential of the circulating microparticles and the microparticle-dependent tissue factor activity were evaluated. A high level of circulating erythrocyte- and platelet-microparticles was found. In contrast, the number of endothelial microparticles was within the normal range. Platelet microparticles were significantly higher in splenectomized than in non-splenectomized patients, independent of platelet count ($P < 0{\cdot}001$). Multivariate analysis indicated that phospholipid-dependent procoagulant activity was influenced by both splenectomy ($P = 0{\cdot}001$) and platelet microparticle level ($P < 0{\cdot}001$). Erythrocyte microparticles were not related to splenectomy, appear to be devoid of proper procoagulant activity and no relationship between their production and haemolysis, dyserythropoiesis or oxidative stress markers could be established. Intra-microparticle labelling with anti-HbF antibodies showed that they originate only partially (median of 28%) from thalassaemic erythropoiesis. In conclusion, when β-thalassaemia major patients are intensively transfused, the procoagulant activity associated with thalassaemic erythrocyte microparticles is probably diluted by transfusions. In contrast, platelet microparticles, being both more elevated and more procoagulant, especially after

splenectomy, may contribute to the residual thrombotic risk reported in splenectomized multi-transfused β-thalassaemia major patients.

Date	Nov 2015
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 4
Volume	171
Pages	615-624
Publication	British Journal of Haematology
DOI	[10.1111/bjh.13609](https://doi.org/10.1111/bjh.13609)
Numéro	4
Abrév. de revue	Br. J. Haematol.
ISSN	1365-2141
Date d'ajout	13/12/2021 10:35:07
Modifié le	13/12/2021 10:35:07

- **Marqueurs :**
  - Blood Platelets
  - Humans
  - Cell-Derived Microparticles
  - Flow Cytometry
  - risk
  - Adolescent
  - Adult
  - Female
  - Male
  - Thrombophilia
  - Middle Aged
  - Phosphatidylserines
  - Membrane Lipids
  - Oxidative Stress
  - Young Adult
  - Autoantibodies
  - beta-Thalassemia
  - Blood Transfusion
  - Combined Modality Therapy
  - Diabetes Mellitus
  - Erythrocyte Membrane
  - erythrocytes derived-microparticles
  - Fetal Hemoglobin
  - Hypogonadism
  - Iron
  - Iron Overload
  - platelets-derived microparticles
  - splenectomy

- Transfusion Reaction
- β-thalassaemia major

Pièces jointes

- PubMed entry

- ## Neutrophils recruit and activate human endothelial colony-forming cells at the site of vessel injury via P-selectin glycoprotein ligand-1 and L-selectin

Type de document	Article de revue
Auteur	L. Hubert
Auteur	R. Darbousset
Auteur	L. Panicot-Dubois
Auteur	S. Robert
Auteur	F. Sabatier
Auteur	K. Fallague
Auteur	F. Dignat-George
Auteur	C. Dubois
Résumé	BACKGROUND: Endothelial colony-forming cells (ECFCs) represent a subpopulation of circulating endothelial progenitor cells that have been implicated in vascular repair. However, no study has evaluated the role of ECFCs in endothelial injury leading to thrombus formation. OBJECTIVE: We investigated the kinetics, mechanisms and role of ECFC recruitment in the dynamics of thrombus formation and stabilization. METHODS AND RESULTS: Using digital intravital microscopy in living mice, we show that ECFCs, but not mature endothelial cells, adhere to sites of laser-induced injury and do not affect the kinetics of thrombus formation. This interaction occurs once the platelet thrombus has been stabilized, and is dependent on the presence of neutrophils but not platelets or fibrin. In vitro, the interaction of the activated neutrophils with activated endothelial cells is a prerequisite for the capture of ECFCs. Neutrophils activate ECFCs and increase their angiogenic properties, such as their ability to migrate and to form pseudocapillaries. This newly identified interaction of ECFCs with the neutrophils is mediated by the P-selectin glycoprotein ligand-1 (PSGL-1)/L-selectin axis both in vitro and in vivo. CONCLUSIONS: This study is the first demonstration that neutrophils present at the site of injury recruit ECFCs via PSGL-1/L-selectin. This interaction between neutrophils and ECFCs could play a key role in the regeneration of injured vessels in pathophysiologic conditions.
Date	Jul 2014
Langue	eng
Catalogue de bibl.	PubMed

Extra	Number: 7
Volume	12
Pages	1170-1181
Publication	Journal of thrombosis and haemostasis: JTH
DOI	10.1111/jth.12551
Numéro	7
Abrév. de revue	J. Thromb. Haemost.
ISSN	1538-7836
Date d'ajout	13/12/2021 10:35:20
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- ### Marqueurs :
  - Blood Platelets
  - Endothelium, Vascular
  - Humans
  - Flow Cytometry
  - Animals
  - Endothelial Cells
  - Thrombosis
  - Neutrophils
  - Cell Adhesion
  - Mice
  - Stem Cells
  - Fibrin
  - RNA, Small Interfering
  - Wound Healing
  - Membrane Glycoproteins
  - Endothelium
  - animal models
  - Fetal Blood
  - hematopoietic stem cells
  - L-Selectin
  - Lasers
  - Leukocytes, Mononuclear
  - Mice, Inbred C57BL
  - Microscopy
  - platelet

  Pièces jointes

  - PubMed entry

- ## Accelerated senescence of cord blood endothelial progenitor cells in premature neonates is driven by SIRT1 decreased expression

Type de document	Article de revue
Auteur	Paula Frizera Vassallo
Auteur	Stéphanie Simoncini
Auteur	Isabelle Ligi
Auteur	Anne-Line Chateau
Auteur	Richard Bachelier
Auteur	Stéphane Robert
Auteur	Julia Morere
Auteur	Samantha Fernandez
Auteur	Benjamin Guillet
Auteur	Maxime Marcelli
Auteur	Edwige Tellier
Auteur	Alain Pascal
Auteur	Umberto Simeoni
Auteur	Francine Anfosso
Auteur	Frédérique Magdinier
Auteur	Françoise Dignat-George
Auteur	Florence Sabatier
Résumé	Epidemiological and experimental studies indicate that early vascular dysfunction occurs in low-birth-weight subjects, especially preterm (PT) infants. We recently reported impaired angiogenic activity of endothelial colony-forming cells (ECFCs) in this condition. We hypothesized that ECFC dysfunction in PT might result from premature senescence and investigated the underlying mechanisms. Compared with ECFCs from term neonates (n = 18), ECFCs isolated from PT (n = 29) display an accelerated senescence sustained by growth arrest and increased senescence-associated β-galactosidase activity. Increased p16(INK4a) expression, in the absence of telomere shortening, indicates that premature PT-ECFC aging results from stress-induced senescence. SIRT1 level, a nicotinamide adenine dinucleotide-dependent deacetylase with anti-aging activities, is dramatically decreased in PT-ECFCs and correlated with gestational age. SIRT1 deficiency is subsequent to epigenetic silencing of its promoter. Transient SIRT1 overexpression or chemical induction by resveratrol treatment reverses senescence phenotype, and rescues in vitro PT-ECFC angiogenic defect in a SIRT1-dependent manner. SIRT1 overexpression also restores PT-ECFC capacity for neovessel formation in vivo. We thus demonstrate that decreased expression of SIRT1 drives accelerated senescence of PT-ECFCs, and acts as a critical determinant of the PT-ECFC angiogenic defect. These findings lay new grounds for understanding the increased cardiovascular risk in individuals born prematurely and open perspectives for therapeutic strategy.
Date	Mar 27, 2014
Langue	eng

Catalogue de bibl.	PubMed
Extra	Number: 13
Volume	123
Pages	2116-2126
Publication	Blood
DOI	[10.1182/blood-2013-02-484956](https://doi.org/10.1182/blood-2013-02-484956)
Numéro	13
Abrév. de revue	Blood
ISSN	1528-0020
Date d'ajout	13/12/2021 10:35:21
Modifié le	13/12/2021 10:35:21

- ### Marqueurs :
    - Humans
    - Endothelial Cells
    - Cells, Cultured
    - Case-Control Studies
    - Cellular Senescence
    - Infant, Newborn
    - Premature Birth
    - Sirtuin 1
    - Fetal Blood
    - hematopoietic stem cells
    - Down-Regulation
    - Infant, Premature
    - Stress, Physiological

  ### Pièces jointes

    - PubMed entry
    - Texte intégral

- ## Soluble melanoma cell adhesion molecule (sMCAM/sCD146) promotes angiogenic effects on endothelial progenitor cells through angiomotin

Type de document	Article de revue
Auteur	Jimmy Stalin
Auteur	Karim Harhouri
Auteur	Lucas Hubert
Auteur	Caroline Subrini
Auteur	Daniel Lafitte

Auteur	Jean-Claude Lissitzky
Auteur	Nadia Elganfoud
Auteur	Stéphane Robert
Auteur	Alexandrine Foucault-Bertaud
Auteur	Elise Kaspi
Auteur	Florence Sabatier
Auteur	Michel Aurrand-Lions
Auteur	Nathalie Bardin
Auteur	Lars Holmgren
Auteur	Françoise Dignat-George
Auteur	Marcel Blot-Chabaud
Résumé	The melanoma cell adhesion molecule (CD146) contains a circulating proteolytic variant (sCD146), which is involved in inflammation and angiogenesis. Its circulating level is modulated in different pathologies, but its intracellular transduction pathways are still largely unknown. Using peptide pulldown and mass spectrometry, we identified angiomotin as a sCD146-associated protein in endothelial progenitor cells (EPC). Interaction between angiomotin and sCD146 was confirmed by enzyme-linked immunosorbent assay (ELISA), homogeneous time-resolved fluorescence, and binding of sCD146 on both immobilized recombinant angiomotin and angiomotin-transfected cells. Silencing angiomotin in EPC inhibited sCD146 angiogenic effects, i.e. EPC migration, proliferation, and capacity to form capillary-like structures in Matrigel. In addition, sCD146 effects were inhibited by the angiomotin inhibitor angiostatin and competition with recombinant angiomotin. Finally, binding of sCD146 on angiomotin triggered the activation of several transduction pathways that were identified by antibody array. These results delineate a novel signaling pathway where sCD146 binds to angiomotin to stimulate a proangiogenic response. This result is important to find novel target cells of sCD146 and for the development of therapeutic strategies based on EPC in the treatment of ischemic diseases.
Date	Mar 29, 2013
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 13
Volume	288
Pages	8991-9000
Publication	The Journal of Biological Chemistry
DOI	10.1074/jbc.M112.446518
Numéro	13
Abrév. de revue	J. Biol. Chem.
ISSN	1083-351X

Date d'ajout	13/12/2021 10:35:21
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- **Marqueurs :**
  - Endothelium, Vascular
  - Humans
  - Endothelial Cells
  - Human Umbilical Vein Endothelial Cells
  - Enzyme-Linked Immunosorbent Assay
  - Signal Transduction
  - Stem Cells
  - RNA, Small Interfering
  - Wound Healing
  - Membrane Proteins
  - Collagen
  - CD146 Antigen
  - Angiostatins
  - Capillaries
  - Drug Combinations
  - Gene Silencing
  - Intercellular Signaling Peptides and Proteins
  - Laminin
  - Mass Spectrometry
  - Microscopy, Fluorescence
  - Neovascularization, Pathologic
  - Proteoglycans
  - Recombinant Proteins
  - Spectrometry, Fluorescence

  Pièces jointes

  - PubMed entry
  - Texte intégral

- ## Leukocyte- and endothelial-derived microparticles: a circulating source for fibrinolysis

Type de document	Article de revue
Auteur	Romaric Lacroix
Auteur	Laurent Plawinski
Auteur	Stéphane Robert
Auteur	Loïc Doeuvre
Auteur	Florence Sabatier
Auteur	Sara Martinez de Lizarrondo
Auteur	Anna Mezzapesa
Auteur	Francine Anfosso

Auteur	Aurelie S. Leroyer
Auteur	Pascale Poullin
Auteur	Noémie Jourde
Auteur	Makon-Sébastien Njock
Auteur	Chantal M. Boulanger
Auteur	Eduardo Anglés-Cano
Auteur	Françoise Dignat-George
Résumé	BACKGROUND: We recently assigned a new fibrinolytic function to cell-derived microparticles in vitro. In this study we explored the relevance of this novel property of microparticles to the in vivo situation. DESIGN AND METHODS: Circulating microparticles were isolated from the plasma of patients with thrombotic thrombocytopenic purpura or cardiovascular disease and from healthy subjects. Microparticles were also obtained from purified human blood cell subpopulations. The plasminogen activators on microparticles were identified by flow cytometry and enzyme-linked immunosorbent assays; their capacity to generate plasmin was quantified with a chromogenic assay and their fibrinolytic activity was determined by zymography. RESULTS: Circulating microparticles isolated from patients generate a range of plasmin activity at their surface. This property was related to a variable content of urokinase-type plasminogen activator and/or tissue plasminogen activator. Using distinct microparticle subpopulations, we demonstrated that plasmin is generated on endothelial and leukocyte microparticles, but not on microparticles of platelet or erythrocyte origin. Leukocyte-derived microparticles bear urokinase-type plasminogen activator and its receptor whereas endothelial microparticles carry tissue plasminogen activator and tissue plasminogen activator/inhibitor complexes. CONCLUSIONS: Endothelial and leukocyte microparticles, bearing respectively tissue plasminogen activator or urokinase-type plasminogen activator, support a part of the fibrinolytic activity in the circulation which is modulated in pathological settings. Awareness of this blood-borne fibrinolytic activity conveyed by microparticles provides a more comprehensive view of the role of microparticles in the hemostatic equilibrium.
Date	Dec 2012
Langue	eng
Titre abrégé	Leukocyte- and endothelial-derived microparticles
Catalogue de bibl.	PubMed
Extra	Number: 12
Volume	97
Pages	1864-1872
Publication	Haematologica
DOI	10.3324/haematol.2012.066167

Numéro	12
Abrév. de revue	Haematologica
ISSN	1592-8721
Date d'ajout	13/12/2021 10:35:21
Modifié le	13/12/2021 10:35:21

- **Marqueurs :**
  - Cardiovascular Diseases
  - Endothelium, Vascular
  - Humans
  - Cell-Derived Microparticles
  - Flow Cytometry
  - Leukocytes
  - Fibrinolysis
  - Enzyme-Linked Immunosorbent Assay
  - Cells, Cultured
  - Fibrinolysin
  - Urokinase-Type Plasminogen Activator
  - Case-Control Studies
  - Purpura, Thrombotic Thrombocytopenic
  - Renal Artery
  - Tissue Plasminogen Activator

  Pièces jointes

  - PubMed entry
  - Texte intégral

- ## High-sensitivity flow cytometry provides access to standardized measurement of small-size microparticles--brief report

Type de document	Article de revue
Auteur	Stéphane Robert
Auteur	Romaric Lacroix
Auteur	Philippe Poncelet
Auteur	Karim Harhouri
Auteur	Tarik Bouriche
Auteur	Coralie Judicone
Auteur	Jennifer Wischhusen
Auteur	Laurent Arnaud
Auteur	Françoise Dignat-George

Résumé	OBJECTIVE: Cellular microparticles (MP) are promising biomarkers in many pathological situations. Although flow cytometry (FCM) is widely used for their measurement, it has raised controversies because the smallest MP size falls below the detection limit of standard FCM (sd-FCM). Following recent technological improvements leading to high sensitivity FCM (hs-FCM), our objectives were (1) to evaluate the potential of hs-FCM for extended MP detection, (2) to set up a standardized protocol for MP enumeration, and (3) to compare MP counts obtained with both sensitivity levels. METHODS AND RESULTS: Compared with sd-FCM, hs-FCM displayed improved forward scatter resolution and lower background noise, allowing us to discriminate previously undetectable small MP in plasma samples. Using fluorescent beads with appropriate sizes (0.1/0.3/0.5/0.9 µm) and relative amounts, a new standardized hs-FCM MP protocol was set up and provided reproducible MP counts. Applied to coronary patient samples, it resulted into 8- to 20-fold increases in MP counts as compared with sd-FCM. Interestingly, the ratio between small and large MP varied according to clinical status but also depending on MP subset, suggesting access to new biological information. CONCLUSIONS: Recent improvements in FCM provide access to previously undetectable MP and represent a new opportunity to enhance their impact as biomarkers in clinical practice.
Date	Apr 2012
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 4
Volume	32
Pages	1054-1058
Publication	Arteriosclerosis, Thrombosis, and Vascular Biology
DOI	[10.1161/ATVBAHA.111.244616](https://doi.org/10.1161/ATVBAHA.111.244616)
Numéro	4
Abrév. de revue	Arterioscler. Thromb. Vasc. Biol.
ISSN	1524-4636
Date d'ajout	13/12/2021 10:35:33
Modifié le	13/12/2021 10:35:33

- **Marqueurs :**
  - Humans
  - Particle Size
  - Cell-Derived Microparticles
  - Flow Cytometry
  - Biomarkers
  - Predictive Value of Tests
  - Calibration

- Coronary Disease
- Reproducibility of Results
- Sensitivity and Specificity

Pièces jointes

- PubMed entry

- ## Impact of pre-analytical parameters on the measurement of circulating microparticles: towards standardization of protocol

Type de document	Article de revue
Auteur	R. Lacroix
Auteur	C. Judicone
Auteur	P. Poncelet
Auteur	S. Robert
Auteur	L. Arnaud
Auteur	J. Sampol
Auteur	F. Dignat-George
Résumé	BACKGROUND: Microparticles (MP) are small vesicles of 0.1-1 µm, released in response to activation or apoptosis. Over the past decade, they received an increasing interest both as biomarkers and biovectors in coagulation, inflammation and cancer. Clinical studies were conducted to assess their contribution to the identification of patients at cardiovascular risk. However, among the limitation of such studies, pre-analytical steps remains an important source of variability and artifacts in MP analysis. OBJECTIVES: Because data from the literature are insufficient to establish recommendations, the objective of the present study was to assess the impact of various pre-analytical parameters on MP measurement. These parameters included the type of collection tube, phlebotomy conditions, transportation practices, centrifugation steps and freezing. METHODS: MP were assessed by three methods: flow cytometry using a standardized approach, a thrombin generation test (Calibrated Automated Thrombogram(®)) and a procoagulant phospholipid-dependent clotting time assay (STA(®) - Procoag-PPL). RESULTS: The main results show that the three major pre-analytical parameters which impact on MP-related data are the delay before the first centrifugation, agitation of the tubes during transportation and the centrifugation protocol. CONCLUSIONS: Based on both this work and literature data, we propose a new protocol that needs to be validated on a larger scale before being applied for multicenter studies.
Date	Mar 2012
Langue	eng

Titre abrégé	Impact of pre-analytical parameters on the measurement of circulating microparticles
Catalogue de bibl.	PubMed
Extra	Number: 3
Volume	10
Pages	437-446
Publication	Journal of thrombosis and haemostasis: JTH
DOI	10.1111/j.1538-7836.2011.04610.x
Numéro	3
Abrév. de revue	J. Thromb. Haemost.
ISSN	1538-7836
Date d'ajout	13/12/2021 10:35:39
Modifié le	13/12/2021 10:35:39

- **Marqueurs :**
  - Humans
  - Cell-Derived Microparticles
  - Centrifugation
  - Flow Cytometry
  - Blood Coagulation
  - Anticoagulants
  - Adult
  - Biomarkers
  - Female
  - Male
  - Thrombin
  - Middle Aged
  - Blood Coagulation Tests
  - Time Factors
  - Cryopreservation
  - Freezing
  - Phlebotomy
  - Practice Guidelines as Topic
  - Specimen Handling
  - Young Adult

  Pièces jointes

  - PubMed entry

- # Sterile inflammation of endothelial cell-derived apoptotic bodies is mediated by interleukin-1α

Type de document	Article de revue

Auteur	Yaël Berda-Haddad
Auteur	Stéphane Robert
Auteur	Paul Salers
Auteur	Leila Zekraoui
Auteur	Catherine Farnarier
Auteur	Charles A. Dinarello
Auteur	Françoise Dignat-George
Auteur	Gilles Kaplanski
Résumé	Sterile inflammation resulting from cell death is due to the release of cell contents normally inactive and sequestered within the cell; fragments of cell membranes from dying cells also contribute to sterile inflammation. Endothelial cells undergoing stress-induced apoptosis release membrane microparticles, which become vehicles for proinflammatory signals. Here, we show that stress-activated endothelial cells release two distinct populations of particles: One population consists of membrane microparticles (<1 μm, annexin V positive without DNA and no histones) and another larger (1-3 μm) apoptotic body-like particles containing nuclear fragments and histones, representing apoptotic bodies. Contrary to present concepts, endothelial microparticles do not contain IL-1α and do not induce neutrophilic chemokines in vitro. In contrast, the large apoptotic bodies contain the full-length IL-1α precursor and the processed mature form. In vitro, these apoptotic bodies induce monocyte chemotactic protein-1 and IL-8 chemokine secretion in an IL-1α-dependent but IL-1β-independent fashion. Injection of these apoptotic bodies into the peritoneal cavity of mice induces elevated serum neutrophil-inducing chemokines, which was prevented by cotreatment with the IL-1 receptor antagonist. Consistently, injection of these large apoptotic bodies into the peritoneal cavity induced a neutrophilic infiltration that was prevented by IL-1 blockade. Although apoptosis is ordinarily considered noninflammatory, these data demonstrate that nonphagocytosed endothelial apoptotic bodies are inflammatory, providing a vehicle for IL-1α and, therefore, constitute a unique mechanism for sterile inflammation.
Date	Dec 20, 2011
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 51
Volume	108
Pages	20684-20689
Publication	Proceedings of the National Academy of Sciences of the United States of America
DOI	10.1073/pnas.1116848108
Numéro	51

Abrév. de revue	Proc. Natl. Acad. Sci. U.S.A.
ISSN	1091-6490
Date d'ajout	13/12/2021 10:35:39
Modifié le	13/12/2021 10:35:39

- **Marqueurs :**
  - Humans
  - Cell-Derived Microparticles
  - Animals
  - Endothelial Cells
  - Inflammation
  - Male
  - Human Umbilical Vein Endothelial Cells
  - Chemokine CCL2
  - Mice
  - Apoptosis
  - Mice, Inbred C57BL
  - Autoimmunity
  - Histones
  - Interleukin 1 Receptor Antagonist Protein
  - Interleukin-1alpha
  - Interleukin-8
  - Lupus Erythematosus, Systemic
  - Reperfusion Injury

  Pièces jointes

  - PubMed entry
  - Texte intégral

- ## Short-term very low-calorie diet in obese females improves the haemostatic balance through the reduction of leptin levels, PAI-1 concentrations and a diminished release of platelet and leukocyte-derived microparticles

Type de document	Article de revue
Auteur	O. Morel
Auteur	F. Luca
Auteur	L. Grunebaum
Auteur	L. Jesel
Auteur	N. Meyer
Auteur	D. Desprez
Auteur	S. Robert

Auteur	F. Dignat-George
Auteur	F. Toti
Auteur	C. Simon
Auteur	B. Goichot
Résumé	BACKGROUND: In obesity, metabolic stress and inflammation in injured tissues could favour enhanced shedding of procoagulant microparticles (MPs). At sites of endothelium injury, the swift recruitment of procoagulant leukocyte-derived MPs enables the initiation of blood coagulation and thrombus growth. OBJECTIVES: In obese females, we sought to evaluate the impact of a very low-calorie diet (VLCD) on procoagulant MP levels, fibrinolytic status, inflammation and endothelium damage. METHODS: Circulating biomarkers of vascular damage, fibrinolytic status, platelet activation and inflammation were measured before, 30 and 90 days after starting a short-term VLCD. MPs were measured by flow cytometry and capture assays. Their procoagulant potential was quantified using functional prothrombinase assays and their cellular origin were determined using flow cytometry (endothelium, platelet, leukocyte, lymphocyte and erythrocyte-derived MP) or capture assays. RESULTS: A total of 24 obese females (39 ± 10 years) with a mean body mass index of 35 ± 4 kg m(-2) were prospectively enroled. Procoagulant leukocyte-derived MPs were associated with the waist circumference at baseline (r=0.534; P=0.010) and at 90 days follow-up (r=0.487; P=0.021). At 90 days, weight reduction (-9.8%) was associated with a lowering of blood pressure, improvement of metabolic parameters and a significant reduction of plasminogen activator inhibitor-1 (PAI-1) (-38%), procoagulant platelet-derived MPs (-43%), leukocyte-derived MPs (-28%) and leptin (-32%) levels. CONCLUSION: In obese females, a short-term VLCD results in an overall improvement of the haemostatic balance characterized by the reduction of PAI-levels, diminished release of platelet and leukocyte-derived MPs and a reduction in leptin levels, an adipocyte-derived cytokine.
Date	Dec 2011
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 12
Volume	35
Pages	1479-1486
Publication	International Journal of Obesity (2005)
DOI	10.1038/ijo.2011.19
Numéro	12
Abrév. de revue	Int J Obes (Lond)
ISSN	1476-5497
Date d'ajout	13/12/2021 10:35:40

Modifié le	13/12/2021 10:35:40

- **Marqueurs :**
    - Blood Platelets
    - Endothelium, Vascular
    - Humans
    - Leukocytes
    - Thrombosis
    - Adolescent
    - Adult
    - Biomarkers
    - Blood Coagulation Factors
    - Female
    - Thromboplastin
    - Aged
    - Middle Aged
    - Hemostasis
    - Prospective Studies
    - Plasminogen Activator Inhibitor 1
    - Erythrocytes
    - Young Adult
    - Caloric Restriction
    - Leptin
    - Obesity
    - Weight Loss

  Pièces jointes

    - PubMed entry
    - Texte intégral
- ## Increased levels of microparticles originating from endothelial cells, platelets and erythrocytes in subjects with metabolic syndrome: relationship with oxidative stress

Type de document	Article de revue
Auteur	O. Helal
Auteur	C. Defoort
Auteur	S. Robert
Auteur	C. Marin
Auteur	N. Lesavre
Auteur	J. Lopez-Miranda
Auteur	U. Risérus
Auteur	S. Basu

Auteur	J. Lovegrove
Auteur	J. McMonagle
Auteur	H. M. Roche
Auteur	F. Dignat-George
Auteur	D. Lairon
Résumé	BACKGROUND AND AIMS: The Metabolic Syndrome (MetS) is associated with increased cardiovascular risk. Circulating microparticles (MP) are involved in the pathogenesis of atherothrombotic disorders and are raised in individual with CVD. We measured their level and cellular origin in subjects with MetS and analyzed their associations with 1/anthropometric and biological parameters of MetS, 2/inflammation and oxidative stress markers. METHODS AND RESULTS: Eighty-eight subjects with the MetS according to the NCEP-ATPIII definition were enrolled in a bicentric study and compared to 27 healthy controls. AnnexinV-positive MP (TMP), MP derived from platelets (PMP), erythrocytes (ErMP), endothelial cells (EMP), leukocytes (LMP) and granulocytes (PNMP) were determined by flow cytometry. MetS subjects had significantly higher counts/µl of TMP (730.6±49.7 vs 352.8±35.6), PMP (416.0±43.8 vs 250.5±23.5), ErMP (243.8±22.1 vs 73.6±19.6) and EMP (7.8±0.8 vs 4.0±1.0) compared with controls. LMP and PNMP were not statistically different between groups. Multivariate analysis demonstrated that each criterion for the MetS influenced the number of TMP. Waist girth was a significant determinant of PMP and EMP level and blood pressure was correlated with EMP level. Glycemia positively correlated with PMP level whereas dyslipidemia influenced EMP and ErMP levels. Interestingly, the oxidative stress markers, plasma glutathione peroxydase and urinary 8-iso-prostaglandin F(2) α, independently influenced TMP and PMP levels whereas inflammatory markers did not, irrespective of MP type. CONCLUSION: Increased levels of TMP, PMP, ErMP and EMP are associated with individual metabolic abnormalities of MetS and oxidative stress. Whether MP assessment may represent a marker for risk stratification or a target for pharmacological intervention deserves further investigation.
Date	Sep 2011
Langue	eng
Titre abrégé	Increased levels of microparticles originating from endothelial cells, platelets and erythrocytes in subjects with metabolic syndrome
Catalogue de bibl.	PubMed
Extra	Number: 9
Volume	21
Pages	665-671
Publication	Nutrition, metabolism, and cardiovascular diseases: NMCD
DOI	10.1016/j.numecd.2010.01.004
Numéro	9

Abrév. de revue	Nutr Metab Cardiovasc Dis
ISSN	1590-3729
Date d'ajout	13/12/2021 10:35:55
Modifié le	13/12/2021 10:35:55

- **Marqueurs :**
  - Blood Platelets
  - Humans
  - Cell-Derived Microparticles
  - Flow Cytometry
  - Endothelial Cells
  - Adult
  - Biomarkers
  - Female
  - Male
  - Aged
  - Middle Aged
  - Metabolic Syndrome
  - Tumor Necrosis Factor-alpha
  - Vascular Cell Adhesion Molecule-1
  - Interleukin-6
  - Case-Control Studies
  - Oxidative Stress
  - Erythrocytes
  - Linear Models

  Pièces jointes

  - PubMed entry

- ## More on: calibration for the measurement of microparticles: value of calibrated polystyrene beads for flow cytometry-based sizing of biological microparticles

Type de document	Article de revue
Auteur	S. Robert
Auteur	P. Poncelet
Auteur	R. Lacroix
Auteur	D. Raoult
Auteur	F. Dignat-George
Résumé	PMID: 21645234
Date	Aug 2011
Langue	eng

Titre abrégé	More on
Catalogue de bibl.	PubMed
Extra	Number: 8
Volume	9
Pages	1676-1678; author reply 1681-1682
Publication	Journal of thrombosis and haemostasis: JTH
DOI	10.1111/j.1538-7836.2011.04387.x
Numéro	8
Abrév. de revue	J. Thromb. Haemost.
ISSN	1538-7836
Date d'ajout	13/12/2021 10:35:40
Modifié le	13/12/2021 10:35:40

- ### Marqueurs :
  - Humans
  - Flow Cytometry
  - Microspheres

  ### Pièces jointes

  - PubMed entry

- ## Overcoming limitations of microparticle measurement by flow cytometry

Type de document	Article de revue
Auteur	Romaric Lacroix
Auteur	Stephane Robert
Auteur	Philippe Poncelet
Auteur	Françoise Dignat-George
Résumé	Circulating microparticles are submicron vesicles released from cell membranes in response to activation or apoptosis. Acknowledgment of their role both as markers and pathogenic effectors in thrombosis, inflammation, and the spread of cancer has increased the interest of their measurement in clinical practice. However, assessment of their clinical use is impeded by technological issues. Among the different methodologies available, flow cytometry is the most commonly used technique. This review addresses flow cytometry limitations in microparticle measurement that may be subdivided into three domains: sizing, probing, and counting. This article also covers the various standardization strategies and technological improvements that have been proposed to overcome these limitations. New tools using size-calibrated beads and recent progress in instrumentation have opened new avenues to improve detection of microparticle populations of smaller sizes. Significant optimization in microparticle detection is also

expected from the use of new fluorescent dyes and the establishment of practical recommendations. Finally, absolute counting of microparticles will also benefit from adapted bead-based strategies or, alternatively, from the generalized availability of volumetric systems. Overall, recent technological improvements maintain flow cytometry as a highly competitive analytical method to measure microparticles. Challenging these evolutions in pathological situations is a mandatory step to validate their real impact in clinical practice.

Date	Nov 2010
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 8
Volume	36
Pages	807-818
Publication	Seminars in Thrombosis and Hemostasis
DOI	[10.1055/s-0030-1267034](https://doi.org/10.1055/s-0030-1267034)
Numéro	8
Abrév. de revue	Semin. Thromb. Hemost.
ISSN	1098-9064
Date d'ajout	13/12/2021 10:35:41
Modifié le	13/12/2021 10:35:41

- **Marqueurs :**
  - Blood Platelets
  - Humans
  - Particle Size
  - Cell-Derived Microparticles
  - Flow Cytometry
  - Animals

  Pièces jointes

  - PubMed entry

- ## Standardization of platelet-derived microparticle enumeration by flow cytometry with calibrated beads: results of the International Society on Thrombosis and Haemostasis SSC Collaborative workshop

Type de document	Article de revue
Auteur	R. Lacroix
Auteur	S. Robert

Auteur	P. Poncelet
Auteur	R. S. Kasthuri
Auteur	N. S. Key
Auteur	F. Dignat-George
Auteur	ISTH SSC Workshop
Résumé	PMID: 20831623
Date	Nov 2010
Langue	eng
Titre abrégé	Standardization of platelet-derived microparticle enumeration by flow cytometry with calibrated beads
Catalogue de bibl.	PubMed
Extra	Number: 11
Volume	8
Pages	2571-2574
Publication	Journal of thrombosis and haemostasis: JTH
DOI	[10.1111/j.1538-7836.2010.04047.x](10.1111/j.1538-7836.2010.04047.x)
Numéro	11
Abrév. de revue	J. Thromb. Haemost.
ISSN	1538-7836
Date d'ajout	13/12/2021 10:35:55
Modifié le	13/12/2021 10:35:55

- **Marqueurs :**
    - plasma
    - Blood Platelets
    - Humans
    - Particle Size
    - Cell-Derived Microparticles
    - Flow Cytometry
    - Calibration
    - Reproducibility of Results
    - Platelet Count
    - Chemistry, Clinical

  Pièces jointes

    - PubMed entry

- ## Levels of circulating endothelial progenitor cells are related to uremic toxins and vascular injury in hemodialysis patients

Type de document	Article de revue
Auteur	N. Jourde-Chiche
Auteur	L. Dou
Auteur	F. Sabatier
Auteur	R. Calaf
Auteur	C. Cerini
Auteur	S. Robert
Auteur	L. Camoin-Jau
Auteur	P. Charpiot
Auteur	A. Argiles
Auteur	F. Dignat-George
Auteur	P. Brunet
Résumé	BACKGROUND: Patients suffering from chronic kidney diseases (CKD) exhibit cardiovascular diseases and profound endothelial dysfunction. CKD patients have reduced numbers of endothelial progenitor cells, but little is known about the factors influencing these numbers. OBJECTIVES: Among these factors, we hypothesized that uremic toxins and vascular injury affect endothelial progenitor cells. PATIENTS/METHODS: Thirty-eight hemodialysis patients were investigated and compared with 21 healthy controls. CD34+CD133+ immature progenitors, CD34+KDR+ endothelial progenitors cells (EPC) and myeloid EPC (mEPC) were counted in peripheral blood. Levels of uremic toxins beta(2)-microglobulin, indole-3 acetic acid, indoxylsulfate, p-cresylsulfate and homocysteine were measured. Vascular injury was assessed in hemodialysis (HD) patients by measuring aortic pulse wave velocity and plasma levels of endothelial microparticles. In vitro experiments were performed to study the effect of uremic toxins on apoptosis of progenitor cells. RESULTS AND CONCLUSIONS: CD34+CD133+ immature progenitor cell number was negatively correlated with the levels of uremic toxins beta(2)-microglobulin and indole-3 acetic acid. In vitro, indole-3 acetic acid induced apoptosis of CD133+ cells. These data indicate uremic toxins have a deleterious role on progenitor cells, early in the differentiation process. Moreover, mEPC number was positively correlated with markers of vascular injury-pulse wave velocity and endothelial microparticle levels. This suggests that vascular lesions could stimulate progenitor cell mobilization, even in a context of reduced EPC induced by CKD. In conclusion, uremic toxins and vascular injury appear to affect endothelial progenitor cell biology in CKD.
Date	Sep 2009
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 9
Volume	7

Pages	1576-1584
Publication	Journal of thrombosis and haemostasis: JTH
DOI	[10.1111/j.1538-7836.2009.03540.x](https://doi.org/10.1111/j.1538-7836.2009.03540.x)
Numéro	9
Abrév. de revue	J. Thromb. Haemost.
ISSN	1538-7836
Date d'ajout	13/12/2021 10:35:56
Modifié le	13/12/2021 10:35:56

- ## Marqueurs :
  - Humans
  - Endothelial Cells
  - Female
  - Male
  - Aged
  - Middle Aged
  - Antigens, CD
  - Apoptosis
  - Stem Cells
  - Renal Dialysis
  - AC133 Antigen
  - Antigens, CD34
  - beta 2-Microglobulin
  - Glycoproteins
  - Indoleacetic Acids
  - Kidney Failure, Chronic
  - Peptides
  - Uremia

  ### Pièces jointes

  - PubMed entry

- # CD146 and its soluble form regulate monocyte transendothelial migration

Type de document	Article de revue
Auteur	Nathalie Bardin
Auteur	Marcel Blot-Chabaud
Auteur	Nicolas Despoix
Auteur	Abdeldjalil Kebir
Auteur	Karim Harhouri
Auteur	Jean-Pierre Arsanto
Auteur	Leon Espinosa

Auteur	Pierre Perrin
Auteur	Stéphane Robert
Auteur	Frédéric Vely
Auteur	Florence Sabatier
Auteur	André Le Bivic
Auteur	Gilles Kaplanski
Auteur	José Sampol
Auteur	Françoise Dignat-George
Résumé	OBJECTIVES: During inflammation, cell adhesion molecules are modulated or redistributed for leukocyte transmigration. Among molecules at the interendothelial junction, CD146 is involved in cell-cell cohesion and permeability, but its role in monocyte transmigration is unknown. METHODS AND RESULTS: TNF enhanced CD146 expression at the junction and apical membrane of human umbilical veins endothelial cells (HUVECs) through CD146 synthesis and intracellular store redistribution. In addition, TNF increased the release of a soluble form (sCD146) through a metalloproteinase-dependent mechanism. The redistribution of CD146 to the junction led us to investigate its role in monocyte transmigration using THP1 and freshly isolated monocytes. Evidence that CD146 contributes to monocyte transmigration was provided by inhibition experiments using anti-CD146 antibodies and CD146 siRNA in HUVECs. In addition, sCD146 specifically bound both monocytes and HUVECs and dose-dependently increased monocyte transmigration. Assessment of sCD146 binding on immobilized CD146 failed to evidence any homophilic interaction. Together, our data suggest endothelial CD146 binds heterophilically with a yet unknown ligand on monocytes. CONCLUSIONS: Our results demonstrate that CD146 is regulated by the inflammatory cytokine TNF and that CD146 and sCD146 are both involved in monocyte transendothelial migration during inflammation.
Date	May 2009
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 5
Volume	29
Pages	746-753
Publication	Arteriosclerosis, Thrombosis, and Vascular Biology
DOI	10.1161/ATVBAHA.108.183251
Numéro	5
Abrév. de revue	Arterioscler. Thromb. Vasc. Biol.
ISSN	1524-4636
Date d'ajout	13/12/2021 10:35:56

Modifié le	13/12/2021 10:35:56

- **Marqueurs :**
  - Humans
  - Monocytes
  - Endothelial Cells
  - Inflammation
  - Tumor Necrosis Factor-alpha
  - Cell Line, Tumor
  - CD146 Antigen
  - Chemotaxis
  - Umbilical Veins

  Pièces jointes

  - PubMed entry
  - Texte intégral

- # TRAIL/Apo2L mediates the release of procoagulant endothelial microparticles induced by thrombin in vitro: a potential mechanism linking inflammation and coagulation

Type de document	Article de revue
Auteur	Stéphanie Simoncini
Auteur	Makon-Sébastien Njock
Auteur	Stéphane Robert
Auteur	Laurence Camoin-Jau
Auteur	José Sampol
Auteur	Jean-Robert Harlé
Auteur	Catherine Nguyen
Auteur	Françoise Dignat-George
Auteur	Francine Anfosso
Résumé	Microparticles are small vesicles playing a crucial role in cell communication by promoting prothrombotic and proinflammatory responses. However, the molecular mechanisms underlying their release are still elusive. We previously established that thrombin promoted the generation of endothelial microparticles (EMPs). In the present study, gene profiling identified TRAIL/Apo2L, a cytokine belonging to the tumor necrosis factor-alpha superfamily, as a target of thrombin. Thrombin increased the expression of cell-associated and soluble forms of TRAIL (sTRAIL) in HMEC-1 cells and human umbilical vein endothelial cells (HUVECs). Blocking TRAIL by specific antibodies or by small interfering RNA reduced both the number and the procoagulant activity of EMPs released by thrombin. Consistent with an

involvement of sTRAIL in thrombin-induced EMP release, we showed that (1) exogenously added sTRAIL generated procoagulant EMPs; (2) supernatants from thrombin-stimulated endothelial cells induced EMP release by HMEC-1 cells and HUVECs, whereas those recovered from TRAIL knockdown endothelial cells displayed no effect. TRAIL/TRAIL-R2 complex mediated EMP release by initiating the recruitment of adaptor proteins and the activation of nuclear factor kappaB. Moreover, sTRAIL modulated intercellular adhesion molecule-1 and interleukin-8 expression induced by thrombin by a downstream pathway involving nuclear factor kappaB activation. Our data reveal a novel mechanism controlling EMP release and identify TRAIL as a key partner in the pathway linking coagulation and inflammation elicited by thrombin.

Date	Apr 24, 2009
Langue	eng
Titre abrégé	TRAIL/Apo2L mediates the release of procoagulant endothelial microparticles induced by thrombin in vitro
Catalogue de bibl.	PubMed
Extra	Number: 8
Volume	104
Pages	943-951
Publication	Circulation Research
DOI	10.1161/CIRCRESAHA.108.183285
Numéro	8
Abrév. de revue	Circ. Res.
ISSN	1524-4571
Date d'ajout	13/12/2021 10:35:56
Modifié le	13/12/2021 10:35:56

- **Marqueurs :**
    - Humans
    - Cell-Derived Microparticles
    - Blood Coagulation
    - Endothelial Cells
    - Inflammation
    - Thrombosis
    - Thrombin
    - Cells, Cultured
    - Signal Transduction
    - RNA Interference
    - RNA, Small Interfering
    - Gene Expression Profiling
    - Time Factors
    - Interleukin-8

- Culture Media, Conditioned
- Intercellular Adhesion Molecule-1
- Receptors, TNF-Related Apoptosis-Inducing Ligand
- TNF-Related Apoptosis-Inducing Ligand
- Transcription Factor RelA
- Transfection
- Up-Regulation

Pièces jointes

- PubMed entry
- Texte intégral

- ## Kidney transplantation decreases the level and procoagulant activity of circulating microparticles

Type de document	Article de revue
Auteur	G. Al-Massarani
Auteur	H. Vacher-Coponat
Auteur	P. Paul
Auteur	L. Arnaud
Auteur	A. Loundou
Auteur	S. Robert
Auteur	V. Moal
Auteur	Y. Berland
Auteur	F. Dignat-George
Auteur	L. Camoin-Jau
Résumé	Microparticles (MP) are important players in cardiovascular disorders. Renal transplantation significantly improves the survival of hemodialyzed patients, in part because cardiovascular disease (CVD) progression is lessened. We hypothesized that the beneficial effect of renal transplantation on cardiovascular outcome might involve decreased levels of circulating MP. We evaluated the kinetics of MP subpopulations and their procoagulant activity (MP-PCA) in 52 patients before and 3, 6, 9 and 12 months after graft with reference to 50 healthy controls and we evaluated the impact of cardiovascular complications. During the follow-up, the increased levels of MP observed before graft were significantly decreased and reached normal values with different kinetics according to their cellular origin whereas MP-PCA remained significantly higher than in controls. From multivariate analysis, the levels of MP were negatively correlated with renal function. At 12 months, the decrease in MP and MP-PCA was more pronounced in patients without history of CVD than those with. In conclusion, we demonstrated that renal graft is associated with decreased levels of MP levels and MP-PCA, even more pronounced so in patients without history of CVD. Therefore, we suggest that MP

	lowering could be involved in the vascular dysfunction improvements reported after transplantation.
Date	Mar 2009
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 3
Volume	9
Pages	550-557
Publication	American Journal of Transplantation: Official Journal of the American Society of Transplantation and the American Society of Transplant Surgeons
DOI	10.1111/j.1600-6143.2008.02532.x
Numéro	3
Abrév. de revue	Am. J. Transplant.
ISSN	1600-6143
Date d'ajout	13/12/2021 10:35:56
Modifié le	13/12/2021 10:35:56

- **Marqueurs :**
  - Cardiovascular Diseases
  - Humans
  - Cell-Derived Microparticles
  - Blood Coagulation
  - Female
  - Male
  - Middle Aged
  - Kinetics
  - Time Factors
  - Graft Survival
  - Graft vs Host Disease
  - Immunosuppressive Agents
  - Kidney Transplantation

  Pièces jointes

  - PubMed entry

- ## Standardization of platelet-derived microparticle counting using calibrated beads and a Cytomics FC500 routine flow cytometer: a first step towards multicenter studies?

Type de document	Article de revue

Auteur	S. Robert
Auteur	P. Poncelet
Auteur	R. Lacroix
Auteur	L. Arnaud
Auteur	L. Giraudo
Auteur	A. Hauchard
Auteur	J. Sampol
Auteur	F. Dignat-George
Résumé	BACKGROUND: Platelet microparticles (PMPs) have proved useful to identify patients with vascular risk. However, PMP counting, which is currently done by flow cytometry (FCM), needs to be standardized. OBJECTIVES: The objectives were (i) to standardize FCM settings for PMP counts on a routine instrument (Cytomics FC500) using size-calibrated fluorescent beads; (ii) to determine intra-instrument and inter-instrument reproducibility; and (iii) to establish PMP values in healthy subjects. METHODS: Using a blend of size-calibrated fluorescent beads (0.5 and 0.9 mum) in a fixed numerical ratio (Megamix), we gated PMPs in a restricted size window. To test intra-instrument and inter-instrument reproducibility, annexin V and CD41 coexpression were used to count PMPs in frozen aliquots of the same platelet-free plasma (PFP) over 4 months and in PFP from 10 healthy subjects on three independent flow cytometers. RESULTS: This calibrated-bead strategy allowed full long-term control of the FCM-based microparticle protocol and reproducible PMP counts over time [coefficient of variation (CV) < 10%]. Optimal settings were easily transferred from one instrument to another, using Megamix as a stable template. Similar PMP counts (CV < 12%) were obtained using the three instruments. With such a standardized FCM protocol, PMP values were established in healthy subjects (n = 60) with significantly higher levels in women than in men [median (1st quartile to 3rd quartile): 1775 microL(-1) (1014-3039 microL(-1)) vs. 656 microL(-1) (407-962 microL(-1))]. CONCLUSIONS: The present strategy provides a new option for PMP count standardization and thus opens the way for multicenter studies.
Date	Jan 2009
Langue	eng
Titre abrégé	Standardization of platelet-derived microparticle counting using calibrated beads and a Cytomics FC500 routine flow cytometer
Catalogue de bibl.	PubMed
Extra	Number: 1
Volume	7
Pages	190-197
Publication	Journal of thrombosis and haemostasis: JTH
DOI	10.1111/j.1538-7836.2008.03200.x
Numéro	1

Abrév. de revue	J. Thromb. Haemost.
ISSN	1538-7836
Date d'ajout	13/12/2021 10:35:56
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- **Marqueurs :**
    - Blood Platelets
    - Humans
    - Particle Size
    - Cell-Derived Microparticles
    - Flow Cytometry
    - Microspheres
    - reference standards
    - Calibration
    - Observer Variation

  Pièces jointes

    - PubMed entry

- ## Impact of immunosuppressive treatment on endothelial biomarkers after kidney transplantation

Type de document	Article de revue
Auteur	G. Al-Massarani
Auteur	H. Vacher-Coponat
Auteur	P. Paul
Auteur	A. Widemann
Auteur	L. Arnaud
Auteur	A. Loundou
Auteur	S. Robert
Auteur	Y. Berland
Auteur	F. Dignat-George
Auteur	L. Camoin-Jau
Résumé	Endothelial dysfunction occurs in hemodialysis and kidney-transplanted patients and can be enhanced by immunosuppressive therapy. Circulating endothelial cells (CEC), endothelial microparticles (EMP) and sVCAM-1 provide information on endothelium activation and damage. We compared the impact of two immunosuppressive regimens (CsA/Aza vs. Tac/MMF) on the kinetics of CEC, EMP and sVCAM-1 levels in 52 patients, both before graft and 3, 6, 9 and 12 months after graft, in reference to 50 healthy controls. CEC, EMP and sVCAM-1 levels were significantly decreased 1 year after transplantation (M12) as compared to pretransplant values. At M12,

CEC and sVCAM-1 levels were significantly higher than those of controls whereas EMP reached normal values. Nine months postgraft, lower CEC and normalized EMP levels were found in patients receiving cyclosporine microemulsion/ azathioprine (CsA/Aza) when compared to patients treated with tacrolimus/ mycophenolate mofetil (Tac/MMF). Multivariate analysis evidenced positive correlations between CEC and history of cardiovascular diseases and between EMP and cytomegalovirus infection at M12. In conclusion, our combined analysis of endothelial injury markers confirms the favorable impact of renal transplantation on endothelium, and show that CEC levels discriminate treatment-associated endothelial toxicity. These results enlighten the potential of these noninvasive blood biomarkers in indexing vascular injury and optimize therapeutic options.

Date	Nov 2008
Langue	eng
Catalogue de bibl.	PubMed
Extra	Number: 11
Volume	8
Pages	2360-2367
Publication	American Journal of Transplantation: Official Journal of the American Society of Transplantation and the American Society of Transplant Surgeons
DOI	10.1111/j.1600-6143.2008.02399.x
Numéro	11
Abrév. de revue	Am. J. Transplant.
ISSN	1600-6143
Date d'ajout	13/12/2021 10:36:13
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- **Marqueurs :**
  - Cardiovascular Diseases
  - Endothelium, Vascular
  - Humans
  - Adult
  - Biomarkers
  - Female
  - Male
  - Middle Aged
  - Vascular Cell Adhesion Molecule-1
  - Kinetics
  - Prospective Studies
  - Cohort Studies
  - Immunosuppressive Agents
  - Kidney Transplantation
  - Mycophenolic Acid

    - Tacrolimus

Pièces jointes

    - PubMed entry

- # Activation of plasminogen into plasmin at the surface of endothelial microparticles: a mechanism that modulates angiogenic properties of endothelial progenitor cells in vitro

Type de document	Article de revue
Auteur	Romaric Lacroix
Auteur	Florence Sabatier
Auteur	Agnès Mialhe
Auteur	Agnès Basire
Auteur	Ralph Pannell
Auteur	Hélène Borghi
Auteur	Stephane Robert
Auteur	Edouard Lamy
Auteur	Laurent Plawinski
Auteur	Laurence Camoin-Jau
Auteur	Victor Gurewich
Auteur	Eduardo Angles-Cano
Auteur	Françoise Dignat-George
Résumé	The regulation of plasmin generation on cell surfaces is of critical importance in the control of vascular homeostasis. Cell-derived microparticles participate in the dissemination of biological activities. However, their capacity to promote plasmin generation has not been documented. In this study, we show that endothelial microparticles (EMPs) from tumor necrosis factor alpha (TNFalpha)-stimulated endothelial cells served as a surface for the generation of plasmin. The generation of plasmin involved expression of urokinase-type plasminogen activator (uPA) and its receptor (uPAR) at the surface of EMPs and was further increased by their ability to bind exogenous uPA on uPAR. Plasminogen was activated at the surface of EMPs in a dose-dependent, saturable, and specific manner as indicated by the inhibition of plasmin formation by epsilon-amino-caproic acid (epsilon-ACA) and carboxypeptidase B. EMP-induced plasmin generation affects tube formation mediated by endothelial progenitor cells. However, low amounts of EMPs increased tube formation, whereas higher concentrations inhibited it. Prevention of these effects by inhibitors of either uPA or plasmin underscore the key role of EMP-induced plasmin generation. In conclusion, we demonstrated that EMPs act as vectors supporting efficient plasmin generation and dissemination, a new

	pathway in the regulation of endothelial proteolytic activities with potential involvement in inflammation, angiogenesis, and atherosclerosis.
Date	Oct 01, 2007
Langue	eng
Titre abrégé	Activation of plasminogen into plasmin at the surface of endothelial microparticles
Catalogue de bibl.	PubMed
Extra	Number: 7
Volume	110
Pages	2432-2439
Publication	Blood
DOI	[10.1182/blood-2007-02-069997](https://doi.org/10.1182/blood-2007-02-069997)
Numéro	7
Abrév. de revue	Blood
ISSN	0006-4971
Date d'ajout	13/12/2021 10:36:14
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- **Marqueurs :**
    - Humans
    - Endothelial Cells
    - Protein Binding
    - Receptors, Cell Surface
    - Cell Line
    - Enzyme Activation
    - Fibrinolysin
    - Intracellular Membranes
    - Neovascularization, Physiologic
    - Plasminogen
    - Receptors, Urokinase Plasminogen Activator
    - Stem Cells
    - Urokinase-Type Plasminogen Activator

Pièces jointes

- PubMed entry
- Texte intégral