



**FRENCH SOCIETY OF
VASCULAR BIOLOGY**
INAUGURAL MEETING

14-16 OCTOBER 2026
NOVOTEL MONTE CARLO



BOOK OF ABSTRACTS

ORAL COMMUNICATIONS

French Society of Vascular Biology (SFBVa) – Inaugural Meeting

14–16 October 2026 · Novotel Monte-Carlo, Monaco

18 selected oral communications

Early endothelial activation at the blood–nerve barrier defines a hallmark of ALS

Session: 2026-10-14 (14:30-16:00) - Neurovascular interactions

Ganesh Parameshwar Bhat¹; Santo Diprima²; Cristian G Beccaria³; Paola Podini⁴; Aurora Badaloni¹; Alessia Motta¹; Brambilla Ilaria¹; Luis Martins¹; Stefano de Pretis²; Nilo Riva⁵; Matteo Iannaccone³; Angelo Quattrini⁴; Dario Bonanomi¹

Background: Vascular defects are common in Amyotrophic Lateral Sclerosis (ALS). The prevailing view is that breakdown of the blood–brain and blood–spinal cord barriers contributes to neurodegeneration. Here, we reveal that selective and early vulnerability of peripheral nerve endothelium —manifested as endothelial cell activation and interlinked blood–nerve barrier dysfunction —constitutes a core feature of ALS pathogenesis, arising before vascular alterations in the central nervous system (CNS) and overt motor neuron pathology.

Results: Vascular changes in ALS patients have been largely studied in postmortem samples, limiting insight into their onset, causes and pathogenic role. Surveying diagnostic motor nerve samples from ALS patients across clinical stages, we observed endothelial damage that preceded overt axonal loss marking vascular dysfunction as an early disease event. Similar ultrastructural abnormalities were detected in pre-symptomatic ALS mouse models (*SOD1* and *TARDBP* mutants). Notably, endothelial cells became dysfunctional even when not carrying mutant TDP-43, indicating they respond to non-cell autonomous disease signals. Transcriptional, histological, and functional analyses revealed that these alterations were largely confined to peripheral nerves, while spinal cord vessels exhibited delayed and more focal changes. Single-cell sequencing identified ALS-susceptible endothelial cell subsets prone to a pro-inflammatory phenotype and impaired blood–nerve barrier function, increasing permeability via the transcellular route. These changes coincided with reactivity of nerve-resident macrophages and neutrophil infiltration. Neutrophil depletion attenuated endothelial activation and barrier leakiness, mitigating axonopathy in ALS mice.

Conclusion: Our work unmasks the greater susceptibility of the peripheral nerve vasculature in ALS relative to the CNS. The early activation of peripheral nerve endothelium, combined with its potential reversibility, identifies a therapeutic window and suggests strategies for targeting the vascular–immune axis to protect the motor system.

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Role of TRIM47/NRF2 pathway in cerebral small vessel disease pathophysiology

Session: 2026-10-14 (14:30-16:00) - Neurovascular interactions

Camille GRENIER¹; Claire PEGHAIRE¹

Background: Cerebral small vessel disease (cSVD) is a chronic and progressive vascular condition for which no specific mechanism-based treatments are currently available. cSVD is a leading cause of strokes (25%) and a major contributor to dementia (45%) [1]. Growing evidence suggests that blood-brain barrier (BBB) dysfunction may play a significant role in the pathogenesis of cSVD. However, our understanding of the underlying disease mechanisms remains limited. Genome-wide and whole-exome association studies have previously identified an association between a variant at the *TRIM47* locus and MRI features of cSVD [2]. TRIM47 is an ubiquitin ligase that is highly expressed in brain endothelial cells (ECs), indicating its potential role in BBB function. Previous *in vitro* data from our lab indicate that TRIM47 displays antioxidant properties in human brain ECs (HBMEC) through its cooperation with NRF2, inducing the expression of NRF2-dependent genes. *In vivo* approach, using *Trim47* full knockout mouse revealed that *Trim47* mutant mice showed lower performances at behaviour tests (water/Y maze), associated with brain defects (astrocytes activation, increased BBB permeability) and decreased activation of the NRF2 pathway in brain ECs [3].

Hypothesis: The reactivation of NRF2 pathway could improve vascular and cognitive functions in *Trim47* mutant mice

Results: Pharmacological activation of the NRF2 pathway with tert-butylhydroquinone or dimethyl fumarate prevented cognitive impairments of *Trim47* knockout mice and rescued the NRF2 pathway, underscoring the role of endothelial TRIM47 in maintaining brain homeostasis via NRF2 signaling and highlighting the translational potential of dimethyl fumarate, an approved human therapeutic.

Conclusion: Our results highlight the key role of TRIM47 as a novel actor of brain physiology and provide a proof of concept of the relevance of targeting the protective antioxidant TRIM47/NRF2 axis in patients with cSVD.

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Endothelial PRDM16 limits infarct growth by maintaining cerebrovascular function during ischemic stroke.

Session: 2026-10-14 (16:30-17:45) - Vascular Brain diseases (from stroke to cancer)

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Background: During ischemic stroke, several cerebrovascular adaptations occur, including alterations in blood-brain barrier (BBB) permeability as well as recruitment of collateral arteri(ol)es, both determinants for stroke outcome. Understanding the mechanisms that govern the function of collaterals and the BBB upon stroke is crucial to establish new therapies. Recently, our host lab has found that transcription factor PRDM16 in arterial endothelial cells (ECs) supports the functionalization of collaterals during hindlimb ischemia. Whether EC-PRDM16 plays a (similar) role in other ischemic diseases, such as ischemic stroke, is unknown.

Hypothesis: In this study, we hypothesize that PRDM16 has a protective role during ischemic stroke by preserving cerebrovascular function of both the BBB and collateral networks.

Results: While many tissues feature an arterial-restricted vascular expression pattern for PRDM16, we demonstrate that PRDM16 expression in the brain vasculature is not limited to arteri(ol)es, but is also present in BBB capillaries. In support of a protective role for PRDM16, we show that EC-specific PRDM16 loss worsened infarct growth during ischemic stroke. PRDM16 loss in ECs resulted in decreased BBB integrity after stroke, as demonstrated by reduced levels of BBB junctional proteins and increased Evans blue extravasation and leakage of blood-borne IgG into the brain parenchyma. Additionally, EC-specific PRDM16 deficiency reduced cerebral collateral perfusion towards the ischemic tissue and attenuated arteriolar vasoreactivity following stroke.

Conclusions: Altogether, these data indicate a protective role for PRDM16 in preserving both BBB and collateral function during stroke. Targeting PRDM16 or its downstream mediators may therefore be of interest to improve cerebrovascular function upon ischemic stroke. The next step is to identify downstream mediators that underlie the protective impact of PRDM16 at single-cell resolution in both vascular beds.

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Neurovascular crosstalk between BMP9/ALK1 signaling and central nervous system-specific endothelial pathways

Session: 2026-10-14 (16:30-17:45) - Vascular Brain diseases (from stroke to cancer)

Louane Despas¹; Nicolas Ricard¹; Aude Salomon¹; Sabine Bailly¹; Agnès Desroches-Castan¹

Abstract (2000 Characters including space)

Background: Hereditary hemorrhagic telangiectasia (HHT) is a genetic vascular disorder characterized by arteriovenous malformations affecting vital organs, including the brain. HHT is caused by loss-of-function mutations in the BMP9/ALK1 signaling pathway. Although BMP9/ALK1 is recognized as a key regulator of endothelial quiescence and vascular homeostasis, its contribution to the molecular programs that define the specialized phenotype of brain endothelial cells remains poorly understood. Unlike peripheral endothelial cells, CNS endothelial cells acquire a highly specialized phenotype that supports blood-brain barrier (BBB) formation and function. This phenotype is established through reciprocal interactions with neurons, astrocytes and pericytes within the neurovascular unit and is controlled by signaling pathways that are unique to the CNS microenvironment.

Hypothesis: Our aim is to investigate the crosstalk between BMP9/ALK1 and endothelial specific CNS pathways. To do this, we first studied its interactions with the canonical WNT/ β -catenin signaling, a pathway essential for BBB development and maintenance.

Results: Our preliminary data support that BMP9 affects a non-canonical WNT/ β catenin signaling pathway. Second, in order to identify, in an unbiased manner, molecular pathways affected by endothelial *Alk1* loss, we employed a transcriptomic approach based on bulk RNA sequencing on endothelial cells isolated from brain adult mice carrying an inducible homozygous deletion of *Alk1* (*Alk1*^{IECKO}) specifically in EC. Pathway enrichment analysis revealed axon guidance, and among them Semaphorin/Plexin/Neuropilins signaling, as one of the most significantly dysregulated biological pathways, highlighting the potential involvement of neurovascular guidance mechanisms downstream of BMP9/ALK1 signaling. We are thus currently studying (1) whether this pathway is directly regulated by the BMP9/ALK1 axis, (2) what is its role in brain endothelial cells and (3) does the semaphorin/plexin/neuropilin pathway regulates BMP signaling pathway.

Conclusion: This study aims to provide new insights into the mechanisms linking BMP9/ALK1 signaling to CNS-specific endothelial programs. By investigating the crosstalk between vascular quiescence pathways and neurovascular signaling networks, this work may help to identify novel mechanisms underlying cerebrovascular alterations associated with HHT.

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Reprogramming the Glioblastoma innate immunity to normalize immune and vascular microenvironments and potentiate chemo- and immune-therapies targeting Sema3a-nrp1-plexina1 Signaling

Session: 2026-10-14 (16:30-17:45) - Vascular Brain diseases (from stroke to cancer)

Jose Sanchez Collado¹; Teo Leboucq¹; Wilfried Souleyreau¹; Annamaria Regina¹; Amélie Germond¹; Andreas Bikfalvi¹; Lucie Brisson¹; Ahmad Sharanek¹; Thomas Mathivet¹

Background: Vascular dysmorphia and massive accumulation of tumour-supportive macrophages are hallmarks of the immunosuppressed Glioblastoma (GB) microenvironment. Both processes promote tumour progression and hinder delivery of existing therapeutics to combat GB (eg chemo- and immune-therapies). On the one hand, non-uniform oxygen delivery via dysmorphic and leaky tumour vessels leads to hypoxia, which upregulates angiogenic factors and thereby creates a vicious cycle that prevents delivery of cytotoxic agents to kill tumour cells. On the other hand, infiltration of immunosuppressive myeloid cells combined with the minimal recruitment of T cells limits the success of currently available T cell-oriented immunotherapies

Hypothesis: The axon guidance factor Sema3A, via its binding to Neuropilin1 and PlexinAs receptors, has been described as both an angiogenic regulator and a myeloid cells phenotypic polarizer. Following these results, we aimed at investigating the role of Sema3A-Nrp1-PlexinA1 pathway over glioma progression in the different cell compartments of the tumor, and the subsequent potentiation of chemo- and immune-therapeutic agents.

Results: Here we show that the secreted guidance factor Sema3A drives glioma progression by i) inducing blood vessel dysmorphia and ii) recruitment of immunosuppressive myeloid cells, depriving the tumour microenvironment of cytotoxic T cells, favouring T cells exhaustion. *In vivo* longitudinal analysis of a syngeneic mouse GB models showed that Sema3A depletion in tumour cells re-educated the tumour stroma and reduced glioma growth by inducing vasculature normalization and accumulation of cytotoxic immune cells. Therapeutically, Sema3A neutralization shifted the tumour microenvironment and resulted in a robust blockade of mouse GB progression and tumor bearing mice survival that was further enhanced by chemotherapy and triple immunotherapy, targeting PD1, CTLA4 and LAG3 pathways.

Conclusion: These data reveal Sema3A as a novel regulator of the GB microenvironment and a potential therapeutic target to treat brain tumours.

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Hyperglycemia disrupt the endothelial primary cilium mechanosensor through AGE/RAGE pathway

Session: 2026-10-15 (09:00-10:30) - Vascular Heterogeneity in health and disease

Anne Darmon¹; Caroline Camare¹; Nicole Malet¹; Kevin Cormier¹; Nathalie Augé¹; Natalia Smirnova¹; Alexandra Montagner¹; Damien Ramel¹; Stephanie Gayral¹; Muriel Laffargue¹

Abstract (2000 Characters including space)

Background: Hyperglycemia, the hallmarks of diabetes mellitus, is a major risk factor for endothelial dysfunction leading to severe vascular complications, notably the initiation of atherosclerosis, the most underlying cause of cardiovascular disease.

Hypothesis: We and others have demonstrated that the primary cilium (PC), a mechanosensory organelle is specifically located on the surface of endothelial cells (ECs), in the low shear stress (LSS) atheroprone regions and plays a key role in preventing endothelial dysfunction and atherosclerosis development¹. However, the impact of diabetes, and especially hyperglycemia, on endothelial PC fate and function has not yet been explored.

Results: To explore the impact of hyperglycemia on endothelial primary cilia, we established a streptozotocin-induced model of hyperglycemia in ApoE^{-/-} mice (40mg/kg for 5 days). We observed a decrease in endothelial PC number in LSS regions, suggesting that hyperglycemia may be responsible for endothelial deciliation. To model chronic exposition to hyperglycemia *in vitro*, EC were exposed to 1 g/L or 5 g/L glucose for 3 days under flow conditions mimicking LSS and we count fewer endothelial EC under high glucose conditions. We further demonstrated that pyridoxamine, an inhibitor of advance glycation end products (AGE) formation arising secondary to hyperglycamia, prevented hyperglycemia-induced PC loss, supporting a role for AGEs in this process. Conversely, ECs exposed to LSS treated with glycating agents such as glyoxal (GO) or methylglyoxal (MGO), presented a reduced number of PC, indicating a role for AGEs in PC loss. We then hypothesized that AGEs acts through the AGE receptor (RAGE) in EC. Thus, hyperglycemic ApoE^{-/-} mice were injected with azeliragon, a RAGE antagonist and we observed that this treatment fully restored PC. Consistently, this protective effect was confirmed *in vitro* with azeliragon and FPS-ZM1, another RAGE inhibitor. Altogether, our results demonstrate that hyperglycemia induces endothelial PC disruption in LSS regions through an AGE/RAGE-dependent mechanism. The molecular pathways underlying this process are currently under investigation.

Conclusion: These findings highlight the impact of diabetes on endothelial mechanosensors and underscore the central role of PC maintenance in the endothelial response to metabolic stress.

1. Nasr M, et al., ATVB, 2024; PMID: 38152888

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The role of ARHGEF18 in endothelial physiopathology: regulation of inflammation and vascular reactivity

Session: 2026-10-15 (09:00-10:30) - Vascular Heterogeneity in health and disease

Ibtissam Babahnini¹; Céline Baron-Menguy¹; Surya Prakash Rao Batta¹; Paul-Louis Rouquette¹; Antoine Rimbert¹; Gervaise Loirand¹; Anne-Clémence Vion¹

Background: The shear stress (SS) generated by the blood flow plays a key role in regulating endothelial cells (ECs) functions and maintaining vascular homeostasis. ECs are designed to adapt to these mechanical forces and an altered perception or response leads to vascular diseases such as atherosclerosis or intracranial aneurysm (ICA). Fine tuning of the cytoskeleton organization and activity is essential to transform the mechanical input into a chemical response and is maintained through the activity of Rho proteins and their upstream activators, the guanine exchange factors (RhoGEF). Recently, our team has identified ARHGEF18 as a mechanosensitive RhoGEF in ECs, interacting with ZO-1 at tight junctions and controlling vascular permeability during developmental processes¹.

Hypothesis: Based on these findings, we hypothesized that endothelial ARHGEF18 may plays a role in maintaining vascular homeostasis in mature arteries.

Results: By characterizing endothelial *Arhgef18* deficient mice (*Arhgef18* iEC-KO) at adulthood, we observed a slight but significant increase in their systolic blood pressure (BP) compared to controls (*Arhgef18*^{lox/lox}). Interestingly, a recent genome wide analysis study (GWAS) identified single nucleotide polymorphisms (SNPs) located along the ARHGEF18 gene, with specific allelic variants associated with a reduced risk of hypertension². However, their impact on *Arhgef18* gene expression has not yet been studied. One of the basic mechanisms regulating BP is the ability of a resistance artery to dilate in response to flow by producing vasoactive molecules such as nitric oxide or prostacyclin. We thus measured *ex vivo* this property and observed a reduced flow-mediated dilation (FMD) of cerebral arteries from *Arhgef18* iEC-KO mice compared to controls. In contrast, contractile properties of *Arhgef18* iEC-KO arteries, linked to their smooth muscle cell function, remain intact. Interestingly, *in vitro* ARHGEF18-deficient ECs exposed to SS had a reduced expression of COX2 gene, one of the key enzymes responsible for prostacyclin production. These ECs also presented a reduced expression of two regulators of inflammation, ICAM1 and CCL2, compared to control. This effect was observed both under SS and static conditions suggesting that the regulation of these genes by ARHGEF18 is independent of flow. Altogether, these findings led us to question the potential role of ARHGEF18 in the context of intracranial aneurysm (ICA), a cerebrovascular disease associated with hypertension, local vascular inflammation and permeability. We thus induced ICA formation on our mice model. Our first analyses revealed the same level of severity of the pathology at the anatomical level (artery diameter and tortuosity) in both groups. Cellular (inflammatory cells recruitment) and molecular (junction stability/COX2 pathway) analyses are currently ongoing to refine our observation.

Conclusion: In conclusion, here we identified a new effect of ARHGEF18 in ECs biology, independent of its activation by flow. ARHGEF18 regulates the physiological level of COX2 expression and two markers of inflammation ICAM1 and CCL2. *In vivo*, endothelial *Arhgef18* deficient mice present a slight increase in blood pressure and a reduced FMD of their arteries compared to controls, in line with human GWAS data.

1. Batta, Surya Prakash Rao et al. "ARHGEF18 is a flow-responsive exchange factor controlling endothelial tight junctions and vascular leakage." *Cell reports* 44,3 (2025): 115288. doi:10.1016/j.celrep.2025.115288
2. Keaton, Jacob M et al. "Genome-wide analysis in over 1 million individuals of European ancestry yields improved polygenic risk scores for blood pressure traits." *Nature genetics* 56,5 (2024): 778-791. doi:10.1038/s41588-024-01714-w

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Translational Research on ACTA2-related Hereditary Thoracic Aortic Aneurysms and Dissections (HTAAD) Rare Disease

Session: 2026-10-15 (09:00-10:30) - Vascular Heterogeneity in health and disease

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Background: ACTA2-related aortic disease accounts for 14% of non-syndromic hereditary thoracic aortic aneurysm and dissection (nsHTAAD) cases. The ACTA2 gene encodes α -actin, a vascular smooth muscle cell (VSMC) protein critical for mechano-transduction, mediating interactions between actin-myosin filaments and the extracellular matrix (ECM), and regulating contractile gene transcription. Clinical practice is challenging due to variable penetrance of ACTA2 pathogenic variants, with the exception of the highly penetrant p.R179X variant. This variant causes multisystemic smooth muscle dysfunction syndrome (MSMDS), a rare disorder characterized by congenital smooth muscle dysfunction affecting the aorta, cerebrovasculature, intestines, lungs and bladder. Recently, newly identified variants classified as “MSMDS-like” exhibit overlapping phenotypic features, like the variant p.G148R, complicating diagnosis and treatment.

Hypothesis: We hypothesized that the location of ACTA2 variant and genetic background may cause distinct functional alterations, resulting in diverse clinical manifestations in patients. To explore this, we used a VSMC model derived from human induced pluripotent stem cells (hiPSC) carrying these ACTA2 variants. Functional analyses assessed cytoskeleton organization, proliferation, migration, contraction and transcriptome profiles in hiPSC-derived VSMCs models.

Results: Our findings demonstrate that p.R179H/+ and p.G148R/+ VSMCs exhibit reduced contractile capacity compared to controls. p.R179H/+ VSMCs also exhibit increased migration, accompanied by transcriptomic downregulation of pathways involved in differentiation and upregulation of genes involved in ECM organization. In contrast, p.G148R/+ VSMCs have an impaired migration, using wound healing assay, compared to controls, accompanied by transcriptomic downregulation of genes involved in ECM organization, wound healing and differentiation.

Conclusion: Ours findings indicate that p.R179H/+ VSMCs exhibit a more synthetic phenotype while p.G148R/+ VSMCs appear less mature. These results highlight the ability of our hiPSC-derived VSMC model to discriminate variant-specific ACTA2 phenotypes *in vitro*. This platform provides a powerful tool to identify key molecular regulators of VSMC dysfunction and to refine genotype–phenotype correlations in vascular disease.

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Dual CXCR2/DRAK1 Inhibition with RCT002 Suppresses Inflammation and Pathological Angiogenesis in Radiation Maculopathy

Session: 2026-10-15 (11:00-12:30) - New breakthrough in vascular biology and therapeutic

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Background: Radiation maculopathy (RM) is a progressive retinal vascular disease that develops after ocular radiotherapy and represents a major cause of vision loss in patients treated for uveal melanoma. Vascular injury, inflammation, and pathological angiogenesis contribute to disease progression. Current treatments, including anti-VEGF agents, mainly control macular edema but do not target upstream inflammatory pathways driving vascular dysfunction. Recent analyses revealed increased levels of ELR+CXCL chemokines in the aqueous humor of patients with RM, suggesting activation of the CXCR2 inflammatory axis.

Hypothesis: We hypothesized that simultaneous inhibition of CXCR2-mediated inflammatory signaling and DRAK1-associated cell death could modulate retinal vascular injury and pathological angiogenesis. RCT002, a novel topical small-molecule inhibitor targeting CXCR2 and DRAK1, was developed to test this hypothesis.

Results: RCT002 inhibited CXCR2-dependent inflammatory signaling and significantly reduced angiogenic and profibrotic responses in retinal cell models. Treatment decreased oxidative stress, inflammatory cytokine production and protected retinal pigment epithelium and photoreceptor cells from cell death. Following topical eyedrop administration, RCT002 achieved measurable exposure in posterior ocular tissues (retina and choroid). In multiple in vivo models of retinal vascular injury, RCT002 reduced retinal vascular leakage and pathological neovascularization. Importantly, therapeutic activity was confirmed in non-human primates. Repeated topical administration was well tolerated, with no evidence of ocular toxicity.

Conclusion: These findings identify CXCR2-driven inflammation as a key component of radiation-induced retinal vascular injury. Dual inhibition of CXCR2 and DRAK1 with RCT002 modulates inflammatory, angiogenic, and degenerative pathways involved in RM. This approach may represent a novel disease-modifying strategy for radiation maculopathy and other retinal vascular diseases like diabetic macular edema.

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Vascular impairments and new emerging comorbidities in Cystic Fibrosis

Session: 2026-10-15 (11:00-12:30) - New breakthrough in vascular biology and therapeutic

Propanna Bandyopadhyay¹; Louise Gaillard¹; Cotinat Marine¹; Sylvia Merkert²; Mathis Le Claire¹; Mathias Declercq³; Isabelle Corre¹; Christophe Blanquart¹; Martin Ulrich²; Peter Witters³; Lucas TREPS¹

Background: Cystic Fibrosis (or mucoviscidosis, CF) is a multisystemic disease associated with broad systemic complications. Latest therapeutic advances with CFTR modulators increased patient life expectancy >60 years, hence transforming CF into a chronic disease of adulthood. Unfortunately, while ageing, patients with CF (pwCF) develop comorbidities including cardiovascular diseases, diabetes and cancer. The increased risk of developing cancer is likely multifactorial but could relate to the persistent pro-inflammatory state (including vessels) seen in pwCF.

Hypothesis: Our aim was to understand the mechanism linking CFTR impairment, vascular malfunctions, and the onset of cancer in pwCF.

Results: We used scRNA-seq in CF lung explants to characterize vascular heterogeneity and endothelial dysfunction compared to healthy lungs. We also compared iPSC-derived endothelial cells (ECs) from pwCF and healthy donors. Finally, we established a new transgenic mouse model with an inducible EC-restricted Cfr inactivation. We studied neonatal retina vessel development and ectopic tumor models in mice.

We demonstrated that CF models of ECs display a profound pro-inflammatory state and altered angiogenesis traits. Moreover, mirroring our recent findings in liver explants, CF lung scRNA-seq data showed 3 distinct populations of EC upregulating genes involved in inflammation, complement cascade and angiogenesis.

Conclusion: The link between CFTR and cancer risk is clear, but the roles of CFTR during tumorigenesis and the involvement of ECs in this phenomenon is not yet well defined. In this study we started to explore the mechanism by which endothelial CFTR-impairment could contribute to tumor progression via endothelial plasticity and inflammation. Altogether, our data suggest that ECs are no innocent bystander in CF pathology, but rather may be active players of the exaggerated inflammatory phenotype.

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LVRV, a VEGFA splice variant driving angiogenesis, lymphangiogenesis and fibrosis: rationale for a first-in-class anti-LVRV × anti-PD-1 bispecific antibody

Session: 2026-10-15 (11:00-12:30) - New breakthrough in vascular biology and therapeutic

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Background: Current anticancer strategies largely target tumor growth, angiogenesis and immune escape, while other central drivers of disease progression remain therapeutically unexploited. Lymphatic vessel expansion, which enables metastatic spread, and stromal fibrosis, which fosters an immunosuppressive and treatment-resistant niche, are rarely addressed by approved agents. We identified Lymphatic and Vascular Resistance Factor (LVRV), a novel VEGFA splice isoform, as a candidate driver of these resistance mechanisms in clear cell renal cell carcinoma (ccRCC). LVRV is induced by tumor-associated hypoxia and further upregulated upon anti-angiogenic treatment stress.

Hypothesis: We hypothesized that LVRV acts as a multifaceted driver of tumor progression, promoting angiogenesis, lymphangiogenesis and matrix remodeling in parallel, and that antibody-mediated LVRV blockade would simultaneously disrupt these complementary resistance mechanisms in anti-angiogenic-resistant tumors.

Results: A panel of fully human monoclonal antibodies was raised against LVRV. Lead candidates combine nanomolar affinity with high target specificity and functionally neutralize LVRV-driven signaling. In vitro, they limited renal carcinoma cell invasiveness and blocked vascular endothelial cell proliferation and lymphatic endothelial cell sprouting. In vivo, anti-LVRV monotherapy slowed the growth of bevacizumab-resistant renal carcinoma xenografts, reduced tumor blood and lymphatic vessel density, and decreased metastatic dissemination of renal tumors in zebrafish. The same antibodies also lowered collagen deposition, a hallmark of diabetic kidney fibrosis, in a streptozotocin-induced model of diabetes in mice.

Conclusions: LVRV is a multifaceted driver of vascular and lymphatic remodeling, fibrosis and resistance to anti-angiogenic therapy. These results provide a strong rationale for combining LVRV blockade with immune checkpoint inhibition. Building on this, Kekkan Biologics is developing Lyvepodimab, a first-in-class anti-LVRV × anti-PD-1 bispecific antibody, as a differentiated therapeutic strategy for solid tumors, notably ccRCC, with high unmet medical need.

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In-vivo-like sprouting tip cell biology in human microphysiological systems

Session: 2026-10-15 (14:30-16:00) - Vascular Biology during development and angiogenesis

Jennifer Schwarzkopf^{1,2,3}; Katja Meier¹; Souhaila Wüsthoff^{1,4}; Daria Bunina^{1,3}; Holger Gerhardt^{1,2,3}

Background: As the 3R principles gain increasing importance, the development of functional in-vitro organ models has become a critical goal in biomedical research. These models offer a promising alternative to animal testing for drug development, toxicological screening, and applications in regenerative medicine. However, the routine use of organoids is still limited by several key challenges, including the lack of physiological vascularization.

Hypothesis: Here, we develop a vascular organoid model, to study the mechanisms of vascular formation.

Results: Harnessing the intrinsic morphogenetic capacity of vascular endothelial cells, we develop a 3D-capillary model, generated by self-organized sprouting and tubulogenesis. This model allows us to investigate critical processes involved in vasculogenesis and angiogenesis, with a particular focus on vessel maturation and the emergence of endothelial heterogeneity over time.

We further evaluate various sources of endothelial cells, including primary endothelial cells and those derived from induced pluripotent stem cells (iPSCs). In addition, we study the interactions between endothelial cells and mural cells, as well as the organ-specific adaptation of endothelial cells when exposed to tissue-relevant signals, for example, those derived from hepatocytes.

Building on these findings, we have developed a highly functional, mature, perfusable vasculature-on-a-chip platform. This technology enables a wide range of applications, including drug screening in a physiologically relevant, human cell-based three-dimensional environment.

Conclusion: We believe this work represents a major step toward the generation of mature, functional, and perfusable capillary networks for use in advanced tissue and organ models. This innovation not only supports the advancement of human-relevant in-vitro systems but also aligns with ethical research standards by reducing reliance on animal models, ultimately contributing to more predictive and translational biomedical research.

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Blood vessels-on-chip for the study of the effects of anti-cancer therapies on the vascular barrier

Session: 2026-10-15 (14:30-16:00) - Vascular Biology during development and angiogenesis

Ibtihal HEZILI^{1,2}; Mitra Lovelin GOLTUM³; Ana Katrina MAPANAO³; Charles MORITZ⁴; Anne-Laure GAGEZ⁴; David PASQUIER⁴; Cristina MULLER³; Fabrice SONCIN^{1,2}

Abstract (2000 Characters including space)

Background: The vascular system is a complex network of blood vessels that supplies tissues and organs with oxygen and nutrients. In cancer, both the structure and functions of the vasculature are altered indirectly by therapeutic interventions. Among these, radiation therapy (RT) is a cornerstone of cancer treatment which can significantly affect vascular integrity and function. More recently, targeted radionuclides therapy (TRT) has emerged as a promising approach. In TRT, radionuclides that emit β^- particles, such as Lutetium-177, are administered intravenously, circulate through the bloodstream, and selectively accumulate in cancer cells that express the targeted receptors. The radiolabeled compounds therefore deliver localized radiation to tumor tissue while minimizing exposure to surrounding healthy tissues.

Methods: Using microfabrication methods, we designed 3D blood vessels-on-chip (VoC) systems that reconstitute concentric layers of primary endothelial and supportive perivascular cells around an open lumen, as in a native blood vessels [1]. The VoC are used here to study the effects of treatments on the vascular barrier integrity and immune activation, its molecular response in terms of gene expression, as well as the general integrity of the inter-endothelial junctions after exposure to radiation.

Results: Results show a dose-effect response of VoC to X-rays. High doses of X-rays induce vascular hyperpermeability. Immunofluorescent staining of irradiated vessels show a dimmed staining of the intracellular junctions, indicating their disruption, in line with the hyperpermeable phenotype. Similar effects on the vascular permeability and barrier integrity were observed following TRT application with ¹⁷⁷Lu-conjugated compounds at variable exposure times (4h and 24h).

Conclusion: Our results show that systemic and targeted radiotherapies induce high radiation damages on the vascular system and directly affect the integrity and functions of blood vessels.

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Single-cell transcriptional identity of pro- and anti-angiogenic telocyte subsets during infantile hemangioma involution

Session: 2026-10-15 (16:30-18:00) - Vascular Biology in Onco-Pediatrics

François Moisan¹; Pechtimaldjian Léa¹; Mathivet Thomas¹; Ndayisaba Lesa Faith¹; Laanani Faiza¹

Background: Infantile hemangioma (IH) evolves through a proliferative phase of ectopic angiogenesis followed by spontaneous involution driven by vessel regression. Over the past several years, our group has progressively established that stromal telocytes, a perivascular population distinct from endothelial cells and pericytes, are not passive bystanders of this vascular remodeling but active, phase-dependent regulators of it. We first identified aquaporin-1 as a specific marker of IH telocytes and showed that the antitumor efficacy of propranolol depends on crosstalk between telocytes and the lesional endothelium [1]. We then demonstrated that endothelial cells, pericytes, and telocytes each locally synthesize noradrenaline, and that propranolol's antiangiogenic effect is only reproducible in vitro when the three cell types are combined above a threshold noradrenaline concentration [2]. To capture this tri-cellular vascular unit in its native architecture, we developed a tissue-clearing and light-sheet imaging protocol allowing undistorted three-dimensional morphometric reconstruction of the cutaneous vascular network [3]. Applying this tool together with secretome profiling, we recently showed that telocytes switch to an activated, dendritic morphology during spontaneous involution and secrete pentraxin 3, which sequesters FGF2 and drives endothelial pruning [4]. This progressive body of work indicates that telocytes are functionally heterogeneous and phase-dependent, but their transcriptional identity, and in particular what distinguishes a pro-angiogenic from an anti-angiogenic/pruning telocyte state, remains uncharacterized.

Hypothesis: We hypothesize that telocytes encompass distinct pro- and anti-angiogenic subpopulations, and that their activation into a pruning phenotype during regression reflects a specific transcriptional reprogramming that can be resolved at single-cell resolution.

Results: To address this, we are performing single-cell RNA sequencing on uncultured cells freshly dissociated from surgically resected IH samples, sampled across proliferative and involuting phases, without any prior culture step. This design aims to preserve the native transcriptional state of telocytes and to map their heterogeneity directly ex vivo, in order to define the transcriptional signatures distinguishing pro-angiogenic telocytes of the proliferative phase from the pruning-associated, anti-angiogenic telocytes engaged during regression. First UMAPs are under analysis and are expected to identify discrete telocyte subsets and activation-associated markers positioned along the proliferative-to-involuting trajectory.

Conclusions: Resolving the transcriptional identity of pro- versus anti-angiogenic telocyte subsets will clarify the molecular basis of their functional switch during IH regression and may uncover markers or targets relevant beyond IH, to other physiological or pathological settings of vascular remodeling.

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Propranolol targets the ADRB2-AQP1 axis to regulate tumor cell migration and multicellular organization in cutaneous angiosarcoma

Session: 2026-10-15 (16:30-18:00) - Vascular Biology in Onco-Pediatrics

Faiza Laanani¹; Tiphaine Delauney²; Léa Pechtimaldjan¹; Christèle Etchegaray³; Annabelle Collin⁴; François Moisan¹

Abstract (2000 Characters including space)

Background: Cutaneous angiosarcoma is a rare and highly aggressive vascular malignancy characterized by marked heterogeneity, high metastatic potential, and poor response to systemic therapies. Propranolol, a non-selective β -adrenergic receptor antagonist successfully used to treat infantile hemangioma, has shown promising clinical activity in a subset of angiosarcoma patients [1], but the mechanisms underlying its antitumor effects and the variability in patient response remain poorly understood, limiting the identification of biomarkers for patient stratification.

Hypothesis: We hypothesize that β -adrenergic signaling, through the ADRB2-AQP1 axis previously identified as a mediator of propranolol response in vascular tumors [2], regulates angiosarcoma progression primarily by modulating tumor cell migration and multicellular tissue organization rather than cell proliferation, and that these effects can be captured quantitatively through combined live imaging and mathematical modeling.

Results: At the cellular level, live imaging of wound-healing assays is coupled with automated single-cell tracking and quantitative mathematical analysis to characterize migration dynamics, including cell trajectories, velocity, and wound closure kinetics, following propranolol treatment or genetic modulation of ADRB2 and AQP1. At the tissue level, three-dimensional angiosarcoma spheroids are used to investigate changes in tumor morphology and organization. Preliminary results show that propranolol inhibits 2D migration but increases spheroid diameter without affecting proliferation or cell viability, consistent with an effect on tissue organization rather than on cell growth. Quantitative image analysis and mathematical modeling are used to extract robust descriptors of spheroid architecture and structural heterogeneity. These findings will be further studied in vivo using our validated bioluminescent angiosarcoma xenograft models.

Conclusion: By integrating vascular biology, quantitative imaging, and mathematical modeling across complementary experimental models, this work provides a multiscale understanding of how β -adrenergic signaling regulates tumor behavior. Beyond elucidating the mechanisms underlying propranolol response, this interdisciplinary framework may identify quantitative biomarkers of tumor organization and migration to improve patient stratification and support the development of more effective therapeutic strategies for angiosarcoma.

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Deciphering the role of perivascular fibroblast cytonemes in neurovascular unit communication

Session: 2026-10-16 (08:30-09:45) - In vivo molecular imaging

Victor MARIN^{1,2}; Marie-Lise BATS^{1,2}; Pascale DUFOURCQ¹; Romain BOULESTREAU¹; Beatrice JASPARD-VINASSA¹; Thierry COUFFINHAL¹; Cecile DUPLAA¹

Background: The neurovascular unit (NVU) maintains blood-brain barrier (BBB) integrity. Its dysfunction contributes to stroke and cerebrovascular disease. Perivascular fibroblasts (PVFs) are an emerging NVU population enriched for ROR2, a WNT5A co-receptor and planar-cell-polarity (PCP) regulator [1]. WNT5A/ROR2 complexes can signal between cells through specialized structures called cytonemes [2–3].

Hypothesis: PVFs communicate within the NVU through ROR2-modulated cytonemes.

Results: In cultured human brain perivascular cells expressing PVF markers, live imaging revealed long, dynamic, F-actin-rich protrusions compatible with cytonemes, ranging from 5 to >100 µm. ROR2 gain- and loss-of-function experiments, WNT5A stimulation and JNK inhibition showed that the WNT5A-ROR2-JNK/PCP axis controls the number and length of cytonemes. Donor-recipient assays demonstrated a contact-dependent transfer of ROR2-positive membrane puncta to neighbouring cells, associated with PCP activation in recipient cells. Laser-capture microdissection coupled to ultra-low-input proteomics defined a first cytoneme-enriched proteome. Across openly available mouse and human single-cell RNA-seq datasets, we show that the WNT5A-ROR2 axis is conserved within PVFs of the NVU. In vivo, in a COL1A1-CreERT2;mTmG mouse model, individual mGFP+ PVF cytoneme-like protrusions were visualized along penetrating arterioles in the developing postnatal brain vasculature (P11–P28), providing first in situ evidence of these putative intercellular communication structures. (Data shown in attached file)

Conclusion: In cultured PVFs, ROR2-dependent cytonemes enable intercellular transfer of ROR2 and activation of PCP signalling in neighbouring cells. Similar protrusion-like structures are also detected in vivo in the developing brain vasculature. Whether these in vivo protrusions are ROR2-dependent and mediate functional communication with cellular partners of the NVU, thereby contributing to cerebrovascular disease, remains unknown. To address these questions, functional in vivo characterization and super-resolution imaging are ongoing.

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Mechanical compression promotes lymphatic barrier failure and inflammation in lymphedema via a Piezo1–CaMKII–NF-κB axis.

Session: 2026-10-16 (09:45-10:30) - Lymphatic vasculature

Florent Morfoisse³; Roxane Sylvestre³; Maelle Charvoz³; Eric Lacazette⁴; Anne-Catherine Prats³; Yukiko Matsunaga¹; Barbara Garmy-Susini³; Aurélien Bancaud²

Background: Secondary lymphedema is a prevalent and debilitating condition characterized by progressive lymphatic dysfunction, tissue fibrosis, and chronic inflammation. Despite its high clinical burden, the underlying mechanisms remain poorly understood. During disease progression, lymphatic vessels experience distinct mechanical environments, transitioning from early-stage intraluminal pressure-induced dilation to late-stage extraluminal compression driven by fibrotic and adipose tissue accumulation. How these pathological mechanical forces contribute to irreversible lymphatic failure remains unclear.

Hypothesis: To address this, we developed a human lymphatic vessel on-chip model enabling precise control of intra and extraluminal pressures. Using this platform, we show that while vessel dilation induces limited effects, extraluminal compression profoundly disrupts lymphatic integrity, leading to increased permeability, barrier breakdown, and severe junctional disorganization.

Results: Transcriptomic analyses revealed that compression induces a strong pro-inflammatory program in lymphatic endothelial cells (LECs), characterized by activation of both canonical and non-canonical NF-κB pathways, indicating that mechanical stress directly drives inflammatory reprogramming.

Mechanistically, compression triggers a sustained intracellular calcium influx associated with high expression of Piezo1 mechanosensitive ion channels, leading to activation of Ca²⁺/calmodulin-dependent protein kinase II (CaMKII). Notably, pharmacological inhibition of CaMKII not only prevents barrier disruption and preserves junctional integrity, but also suppresses NF-κB-dependent inflammatory activation of LECs under compression. Importantly, these findings are recapitulated in a murine model of secondary lymphedema.

Conclusion: Collectively, our results identify a Piezo–CaMKII–NF-κB mechanotransduction axis linking pathological compression to lymphatic barrier failure and inflammation. This work provides a mechanistic basis for the irreversibility of advanced lymphedema and highlights CaMKII as a promising therapeutic target to protect lymphatic vessels from mechanical injury.

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Translational control and ribosomal RNA 2'-O-methylation under endoplasmic reticulum and genotoxic stress in human lymphatic endothelial cells

Session: 2026-10-16 (09:45-10:30) - Lymphatic vasculature

Mehdi HERHOUR¹

Abstract (2000 Characters including space)

Background: Lymphangiogenesis is an important parameter of cancer progression, as lymphatic vessels facilitate the dissemination of cancer cells and the formation of metastases. In previous reports, we have shown that lymphangiogenic growth factors are mostly induced at the translational level under hypoxic stress [1,2]. This translational regulation occurs by an alternative mechanism as global translation is inhibited under stress conditions. Lymphangiogenic growth factor mRNAs are thus translated following the activation of internal ribosome entry sites (IRESs). IRES elements are structural features present in these mRNAs, that allow internal recruitment of ribosomes. IRES-dependent translation is regulated by IRES trans-acting factors (ITAFs) but also by the ribosome itself, shown to be heterogenous in cells. In particular, changes in ribosomal RNA (rRNA) 2'-O-methylation are associated with activation of IRES-dependent translation during epithelial–mesenchymal transition leading to cell transformation [3].

Hypothesis: In the present study, we focus on translational control and variations in rRNA 2'-O-methylation in human dermal lymphatic endothelial cells (HDLECs) subjected to endoplasmic reticulum (ER) stress induced by tunicamycin or genotoxic stress induced by doxorubicin, a drug widely used in cancer chemotherapy.

Results: We show that IRES-dependent translation, mediated by the IRES elements present in the mRNAs of vascular endothelial growth factor C (VEGFC) and fibroblast growth factor 1 (FGF1), is activated after 4–6 hours of treatment with tunicamycin or doxorubicin. To investigate a potential link with ribosomal modifications, RiboMethSeq experiments were performed on rRNA purified from different fractions of polysome gradients. In the absence of stress, 112 methylated sites are detected, most of which exhibiting methylation levels around 90% (i.e., present in ~90% of ribosomes) in polysomes, 80S ribosomes, and free ribosomal subunits. In contrast, 18 sites show methylation levels ranging from 0 to 80%, varying between polysomes, 80S particles, and free subunits; notably, free subunits are undermethylated compared to ribosomes engaged in translation. These data reveal ribosome heterogeneity in terms of 2'-O-methylation.

Conclusion: Furthermore, both ER and genotoxic stress induce a reversal of this pattern: free subunits become hypermethylated, whereas translating ribosomes become hypomethylated. The mechanistic link between these variations in 2'-O-methylation and IRES-dependent translation is currently under investigation.

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