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REVIEW

JCCS editorial board: a wide array of expertise

Bernard Perbal [1]

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The following captures the JCCS editors' unanimous response to my invitation and to take up the challenge of presenting in about 10 lines and 2 references their main scientific expertise.

Bernard Perbal, Editor in Chief.

The solid training in biochemistry, genetics, and immunology that I received during my studies of bacterial ATCase in the 70s, opened me up to the world of virology with precursor molecular approaches of HSV in 1975, followed by analysis of the tumorigenic potential of papilloma virus and retroviruses. In the early 80's, I developed a unique expertise in DNA manipulation and became one of the cloning pioneers with the molecular cloning of the v-myb oncogene of AMV. My cloning of the MAV (helper of the defective AMV) proviral genome set the stage to our identification of CCN3 in 1992, as an insertional mutagenesis site within the host cell DNA. From that time on, I have been fascinated by the wide array of CCN proteins functions, in spite of their high structural conservation, and I have undertaken structure-function studies to uncover mechanistic aspects underlying this puzzle. I have proposed a combinatorial model of events that may account for these apparently opposite features.

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Andrew Leask, Managing and Section Editor

Dr. Leask is an expert on the role of the microenvironment in driving connective tissue pathologies such as scleroderma and melanoma. He has pioneered the use of fibroblast-specific knockout mice to show that an autocrine, proadhesive signaling loop is both necessary and sufficient to initiate and maintain the fibrotic phenotype and that CCN protein are essential regulators of this loop and are therefore bone fide targets for drug therapy. His work has also shown that the cancer-associated fibroblast, through CCN action, is essential for melanoma metastasis.

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Quesnel K, Shi-wen X, Hutchenreuther J, Xiao Y, Liu S, Peidl A, Naskar D, Siqueira W L, O'Gorman D B, Hinz B, Stratton RJ, Leask A (2019) CCN1 expression by fibroblasts is required for bleomycin-induced skin fibrosis matrix biology plus, 3, 100009

Satoshi Kubota, Section Editor

I have been working with CCN family members, mainly in the field of cartilage and bone biology. Since I started my career as a researcher, I have been particularly interested in gene regulatory systems. Therefore, I started CCN family research from the analysis of post-transcriptional regulation of the CCN2 gene, and this kind of studies are still going on. Later, my research scope was expanded to the molecular function of CCN family proteins in skeletal hard tissues. However, novel RNA molecules discovered by the high speed sequencing are also recently attracting my interest. Five years ago, we did not recognize a vast number or RNA molecules present inside and outside of the cells. Now I am interested in possible roles of such RNAs in cell

communication and signaling, suspecting their interaction with CCN family members.

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Dieter Reinhardt, Section Editor

Dr. Reinhardt is internationally recognized for his contributions to cell-matrix biology as it relates to human disease. The focus of his research program is on extracellular fiber systems, their supramolecular structures, their contributions to cell, tissue and organ function, and their role in disease development and progression. He uses a wide spectrum of research tools including genetic mouse models, as well as cell biological, biochemical, and biophysical approaches. He addresses pertinent questions in connective tissue disorders that affect blood vessels, bone, skin and eyes.

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David Abraham

Interests include the study of Inflammation, the molecular and cellular pathobiology of autoimmune connective tissue diseases, and the genetic and molecular mechanisms underlying tissue scarring and fibrosis. Expertise in deep phenotyping, fibroblast and myofibroblasts biology, and transcriptional control mechanisms and in the development and use of in vivo systems of human disease (transgenic and genetically modified conventional and conditional knock-outs) as preclinical models to study the pathogenesis and treatment of connective tissue diseases

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K. Ravi Acharya

Our research is aimed at elucidating the structure-function relationship of molecules involved in normal and disease processes with a more recent focus on angiogenic molecules (CCN proteins, angiogenin and VEGF family members) and molecules involved in inflammatory processes (toxins), functions in the vascular system such as Angiotensin I converting enzyme (ACE). We have complemented our structural studies using X-ray crystallography in understanding protein-protein/carbohydrate interactions with high-throughput compound library screening, structure based design of inhibitors, computational and biophysical techniques as well as protein engineering, enzyme kinetics, cell and developmental biology approaches. The long term objective of our research is to design new pharmacological agents to treat human diseases.

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Håvard Attramadal

My research group has for more than 10 years focused the research activities on the functional role of CCN2 in the heart, in particular the role of CCN2 in the pathophysiology of myocardial remodeling and fibrosis associated with heart failure. We have also investigated the role of CCN2 as a cardioprotective factor in ischemia-reperfusion injury. Our current research is aimed at deciphering the structure-activity relationships of CCN protein. In a recent report we provide evidence that CCN proteins may be regarded as preproproteins, that require endopeptidase cleavage in order to release the biologically active fragment. The mechanisms that regulate the biologic activity of CCN proteins and their mechanisms of transmembrane and intracellular

signaling are currently major areas of research in our laboratory.

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Patrick Auberger

Dr. Patrick Auberger is a research director at the French National Institute of Health and Scientific Research (Inserm) and also the head of the Mediterranean Center for Molecular Medicine (C3M/InsermU1065) in Nice, France. He is an expert in the field of Oncohematology. His main competences and contributions concern the mechanisms of resistance to chemo, targeted and immunotherapies in hematopoietic malignancies with a special focus on myeloid malignancies. The team headed by Dr. Patrick Auberger investigate the role of apoptosis (caspases) and autophagy (cathepsins) in the differentiation and polarization of monocytes and in the resistance to different therapies in myeloid leukemia. The present project also aims at understanding how targeting apoptosis and autophagy may impact treatment of patients suffering myeloid leukemias.

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Sushanta Banerjee

The subject of research in my laboratory is breast and pancreatic cancers, the primarily metastatic progression of these diseases. We have used modern techniques of molecular biology, genetically engineered mouse models (GEMMs), genetically characterized human breast and pancreatic cancer cell lines, and state-of-the-art imaging techniques. Several of the main projects in our laboratories center around the study of CCN-family proteins, including CCN1 and CCN5, which play critical roles in the regulation of breast and pancreatic cancer. Based on our previous studies, we believe that these two proteins are druggable targets for both breast and pancreatic cancers. Thus, our current goal is to find small molecules to target CCN5 or CCN1 or both to prevent the disease progression.

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George Bou-Gharios

My laboratory have been interested in transcriptional regulation of genes involved in connective tissue diseases. We have identified cell specific elements within the collagen type I that drive expression in fibroblasts which helped us identify a number of genes involved in fibrosis including CCN2. We recently worked on aggrecan and showed several cis-acting sequences that confer expression in different chondrocytes. Our latest endeavour is to look at genes that are involved in osteoarthritis using gain and loss of function and since chondrocyte maturity involves CCN2, we investigated the enhancers within this locus to understand the pathophysiology of osteoarthritis. This remains our current focus using cre-lox system and CRISPR to identify the critical regions within the chondrogenic matrix that influence the onset or progression of this disease.

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Enrique Brandan

The main interest of our laboratory is to understand the molecular mechanisms that Our main interest is to understand the molecular mechanisms that regulate skeletal muscle formation and how they are affected in skeletal muscular dystrophies. Our research has conducted extensive studies to understand the role of the extracellular matrix (ECM) in skeletal muscle formation and regeneration and, in the comprehension of the fibrotic response associated with skeletal muscular dystrophies

The presence of the ECM is essential for normal myogenesis. Under fibrotic conditions, the interaction of ECMs with fibroblasts induces the expression of the profibrotic connective tissue growth factor (CTGF/CCN2). Understanding the role of CTGF/CCN2 and the cell type(s) responsible for the fibrotic response is critical to comprehend their roles and potential targeting to be used in therapeutical approaches.

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Rolf A. Brekken

Dr. Brekken is the Effie Marie Cain Scholar in Angiogenesis Research, Professor & Vice Chair of Research in the the Department of Surgery, Deputy Director of the Hamon Center for Therapeutic Oncology Research and Chair of the Cancer Biology Graduate Program at UT Southwestern. Professor Brekken's laboratory is focused on understanding how the tumor microenvironment effects therapeutic efficacy and influences tumor progression. Epithelial plasticity driven by Axl, Tgfβ and collagen signaling as well as strategies to enhance immune therapy, particularly PS-targeting mAbs, are current areas of focus in the lab.

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David Brigstock

I have a long-standing interest in CCN2 protein biochemistry and the role of CCN2 in liver fibrosis. More recently I have become focused on the role of extracellular vesicles (EVs) such as exosomes in intercellular communication in the liver and the potential value of EV molecular payloads as therapeutic or diagnostic tools for chronic liver injury. I have expertise in the cell and molecular biology of fibrosing liver injury as well as the molecular and biological characterization

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Brahim Chaqour

The research focus in my lab is on the adaptive and maladaptive responses of cells and tissues to mechanical stresses (e.g., stretch, shear stress, stiffness of the extracellular matrix,

pressure overload) and/or chemical insults imparted by hypoxia, hyperoxia, hyperglycemia and/or hyperlipidemia. Our studies involve uncovering genetic, molecular, developmental and pathological mechanisms whereby mechanosensitive genes like those of the CCN family of proteins control vascular circuit formation, regeneration and regression. We use rodent models and multi omic approaches to define the genetic and signaling bases of differences in CCN protein functions in cardiovascular and neurovascular tissues and study their implications in vascular dysfunction and blood barrier breakdown. New information of considerable scientific and therapeutic value is expected to be gained from these studies.

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Mick Dashwood

My research over the last 30 years has focused on mechanisms underlying structural changes to blood vessels used as bypass grafts in heart disease patients. These studies have been performed in both experimental models and in grafts obtained from patients undergoing coronary artery bypass surgery. There is considerable current interest in the beneficial role of the perivascular fat that surrounds most blood vessels, in particular, the protective properties of adipocyte-derived factors. Within the wall of vessels used as bypass grafts is a network of microvessels, the vasa vasorum that provides cells with oxygen and nutrients. Experimentally, occlusion of, or damage to, the vasa vasorum causes vessel wall hypoxia, stimulating the release of a variety of factors detrimental to graft performance. Such a system not only maintains oxygen supply to the graft wall but may allow two way traffic of both 'good' and 'bad' factors via "inside out/outside in communication".

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Gary Fisher

General area of research interest is the molecular mechanisms that cause the decline of organ function during the aging process. This research focuses on 1) age-related alterations of the structure, composition, and mechanical properties of the dermal extracellular matrix in human skin and 2) the impact of these alterations on the functions of cells that reside within the extracellular matrix and the adjacent epithelium. Findings from this research highlight the importance of the extracellular microenvironment in determining age-related alterations of cellular functions. Additional areas of active research include wound healing, photobiology, retinoid signaling, CCN family proteins in cutaneous biology, genetically-modified mouse models of aging, and epithelial-stromal interactions in carcinogenesis. Highlights of the research include elucidating the involvement of matrix metalloproteinases in skin aging and the molecular mechanisms of action of retinoids in the skin.

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Denise Fitzgerald.

My research group is particularly interested in the process of myelin regeneration (remyelination) and aim to identify novel therapeutic targets to promote remyelination in demyelinating diseases such as Multiple Sclerosis (MS). To do this, we are uncovering new knowledge of how the immune system influences tissue regeneration in the Central Nervous System (CNS). We recently discovered a new tissue-regenerative role for regulatory T cells in the CNS, mediated in part, through CCN3 (Dombrowski et al., Nat Neuro, 2017). We also conduct research on the pathogenesis of autoimmune inflammation. This programme mainly focuses on T cell biology with a view to identifying strategies to reduce disease activity in MS and other immune-mediated diseases. Previous work investigated the fundamental biology of IL-27 and its therapeutic potential in inflammatory/autoimmune disease, with

particular focus on Th1- and Th17-mediated inflammatory responses (Fitzgerald et al., Nat Immunol, 2007).

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Roel Goldschmeding

Current research focus is the role of DNA-damage response and cellular senescence in kidney fibrosis and lung fibrosis, including senescence biomarkers and targeted therapy for clearance of senescent cells for the treatment of fibrotic diseases. Consortium leader "TASKFORCE" addressing these issues, consisting of UMCU (Pathology and Nephrology), UU (Pharmacy), RWTH Aachen (Nephrology), EUR (Nephrology). Past research projects resulted in identification of CCN-2 as a key factor in tissue remodeling, establishing its role as a pathway modifier (including TGFβ/BMP), biomarker, and target for therapy in kidney diseases. Previously, I identified major target antigens of anti-neutrophil cytoplasmic antibodies (ANCA), including the serine proteases PR3 and HNE, and developed the first antigen-specific ELISAs improving diagnostics and monitoring of patients with small vessel vasculitides.

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Donald Gullberg

Fibrosis is a pathological response to organ injury and is characterized by proliferation of fibroblasts, their differentiation into myofibroblasts and excessive ECM production and deposition. The presence of myofibroblasts stands out as a common hallmark for fibrotic diseases but also makes this cell type an attractive target for therapeutic approaches in wound healing, chronic fibrosis and cancer(1). We hypothesize that integrin 11 demarcates a pro-fibrotic subpopulation of fibroblasts and in this respect can be a useful biomarker and potentially also a therapeutic target in fibrotic tissues and tumors. Thanks to many years of basic research on integrin 11(2)we have animal models, cell lines and reagents that can be used in basic research enabling mechanistic understanding of how the blocking reagents work in the context of fibrosis. In basic research approaches the challenges in years ahead include understanding how 11 1 integrin regulates fibrosis and determining if 11 reagents can be used to shed light on the role of fibroblast heterogeneity in fibrotic disease.

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Sandra Irvine

My research expertise is in leukaemic stem cells focussed on targeting aberrant apoptotic mechanisms in myeloid leukaemia and Multiple Myeloma. A central tenet of my work is that it has a clear translational slant and we are particularly interested in the development of new therapeutic strategies for resistant disease. The Ubiquitin Proteasome System (UPS) plays a key role in the recognition and degradation of damaged proteins. Proteasome inhibitors have recently become an integral part of targeted therapy in blood cancers. We have carried out UPS microarray studies comparing normal and leukaemic stem cells which identified a number of novel targets on this pathway, upstream of the proteasome, which we are currently in the process of characterising. It is hoped that this will allow us to more specifically kill the leukaemic stem cells whilst sparing normal cells and with fewer side effects for patients.

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Celina Kleer

Celina Kleer is the Harold Oberman Collegiate Professor of Pathology and co-Director of Breast Pathology at the University of Michigan. Her research focuses on understanding mechanisms of aggressive breast cancer and on the discovery of tissue-based biomarkers and therapeutic targets. Main contributions to science are the initial identification of EZH2 overexpression in triple negative breast cancers and elucidation of phospho-EZH2 T367 function in metastasis, and the key role of the matricellular protein CCN6 as tumor suppressor in metaplastic breast carcinomas.

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Akira Kudo

My scientific interest is a matricellular protein, periostin, which I named in 1999

Periostin action has been investigated in incurable diseases, such as myocardial infarction, hypertrophy, allergy, atopy, tumor metastasis and stroke, due to the function in cell migration and fibrillogenesis

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Paul Lasko

Is a James McGill Professor in the Department of Biology at McGill University. He served as Scientific Director of the Institute of Genetics of the Canadian Institutes of Health Research from 2010-2018 And is presently spending a sabbatical year in the Department of Human Genetics at Radboudumc in the Netherlands. Dr. Lasko conducts fundamental research on RNA-dependent genetic processes underlying Drosophila development

A recent example of his work is Dold et al. 2020 PLoS Genetics, PMID 31978041, which identified Makorin-1, a protein conserved in all multicellular eukaryotes, as a sequence-specific RNA binding protein that activates translation by recruiting poly(A) binding protein to a target mRNA. Dr. Lasko has also been highly active in international efforts to foster data sharing and increased collaboration among researchers working in the area of rare genetic diseases. To that end, he serves on the board of directors of the Undiagnosed Diseases Network International, a collaboration established in 2014 that encompasses researchers and patient organizations in 15 countries

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Lester F. Lau

My laboratory has been studying the functions and mechanisms of action of the CCN family of proteins. In recent years we have focused on CCN1 in inflammation, wound healing, and tissue regeneration. We have found that CCN1 regulates the innate immune response to injury, accelerates parenchymal regeneration, and promotes

matrix remodeling for resolution of the granulation tissue in various contexts. These diverse functions underscore the actions of CCN1 through distinct integrin receptors in disparate cell types.

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Jack Lawler

Dr. Lawler's research explores the role of the extracellular matrix in determining cellular phenotype in health and disease. He specifically focuses on the thrombospondins (TSPs), which comprise a family of extracellular, calcium-binding proteins that modulate cellular proliferation, migration and differentiation. His research is focused on the biochemistry, cell biology and genetics of the TSP gene products. His initial biochemical and structural studies have provided a foundation for the subsequent analysis of the structure and function of all five members of the TSP gene family. The type 1 repeats (TSRs) of TSP-1 activate transforming growth factor β, inhibit angiogenesis and serve to guide axons. Dr. Lawler's lab currently focuses on (1) the inhibition of angiogenesis and ovarian cancer progression by recombinant versions of the TSRs, and (2) characterization of the molecular mechanisms for anti-angiogenic signaling in endothelial cells, which vary as the organism ages.

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Zhiyong Lin

The broad scope of Dr. Zhiyong Lin's research program entails the molecular mechanisms that govern cardiovascular function. The breakdown of these processes significantly contributes to the onset and progression of many vascular pathologies. The fundamentals of these vascular diseases, such as atherosclerosis, aortic aneurysm, thrombosis and peripheral artery disease are the major focus of his laboratory with the ultimate goal geared toward the development of strategies for disease prevention and treatment. He has made seminal contributions toward understanding the functions of a family of transcription factors, termed Kruppel-like factors (KLFs), and has helped elucidate their roles in gene regulation, vascular biology, and metabolism. Current efforts are focused on dissecting the regulatory roles the two important signaling regulators: Cellular Communication Network (CCN) factor proteins and Protein phosphatase 2A (PP2A) in cardiovascular function. Specifically, the Lin lab utilizes a variety of in vitro and in vivo disease models complemented with contemporary approaches to decipher mechanistically how these proteins influence cellular and organismal homeostasis. With this work, the lab aims to expand upon the notion that CCNs and PP2A are at critical molecular nodal points that govern cardiovascular health and disease, with the goal of the development of future therapeutic therapies that target these critical proteins.

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Kathryn Meier

Dr. Meier is a molecular pharmacologist with expertise in signal transduction. In particular, she has explored the roles of phospholipid and fatty acid mediators, protein phosphorylation cascades, and G protein-coupled receptors in cancer cell signaling. Her research group has also investigated the roles of CCN family proteins in prostate and breast cancer and in lymphoma.

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Kim Midwood

I have a long-standing interest in defining the molecular mechanisms underlying a successful immune response and understanding how these are compromised in related diseases. My research focuses on investigating how extracellular matrix molecules that are specifically induced upon tissue damage control cell behaviour during inflammation and repair. Combining structural, biochemical, proteomic, and genomic approaches, my lab investigates how matrix molecules create a 3D, pro-inflammatory niche at sites of inflammation enabling cells to proliferate and thrive, how this specialized microenvironment persists in inflammatory diseases, driving chronic inflammation and how this information can be translated into new therapeutic strategies.

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Kohei Miyazono

Kohei Miyazono has long-standing interests in the signaling pathways of transforming growth factor beta (TGF-beta) family and their roles in cancer and vascular diseases. In particular, he is interested in the roles of TGF-beta and bone morphogenetic proteins (BMPs) in various types of cancer, including lung cancer, pancreatic cancer, and glioblastoma

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Joanne Murphy-Ullrich

Dr. Murphy-Ullrich's expertise is in the extracellular matrix (ECM) with a focus on the matricellular protein thrombospondin1 (TSP1). She identified the intermediate adhesive state triggered by TSP1 and its roles in cell-ECM deadhesion, cell migration, and anoikis resistance. Her lab discovered that TSP1 is a major regulator of latent TGF-β activation and established TSP1 as a t factor in regulating TGF-beta activation in numerous diseases and in the tumor microenvironment, leading to development of small molecule antagonists of the TSP1-latent TGF-beta interaction. Her lab also identified calreticulin (CRT) as a regulator of TGF-β signaling, linking ER stress and fibrosis in vascular neointima formation and in diabetic nephropathy. She has held leadership positions in ECM, including President of the American Society for Matrix Biology (2017–2018) and she chair/co-chaired FASEB Scientific Conferences on Matricellular Proteins (2010, 2013, 2019)

References

Murphy-Ullrich JE, Suto MJ. (2018) Thrombospondin-1 regulation of latent TGF-β activation: a therapeutic target for fibrotic disease. Matrix biol. Aug; 68-69:28-43. (PMC6015530)

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Kunimasa Ohta

Dr. Ohta has been studying the molecular signaling at the extracellular region. He has cloned and designated the soluble molecule Tsukushi (TSK), which belongs to the Small Leucine-Rich Proteoglycan (SLRP) family. He showed that TSK is involved in the different developmental processes of multiple vertebrate organisms through the diverse signaling cascades. Recently, his work has also shown the direct interaction between CCN2 and TSK, indicating the existence of CCN-SLRP signaling crosstalk.

References

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Anie Philip

My research focuses on understanding the regulation of transforming growth factor-beta (TGF-beta) signaling pathways and their dysregulation in diseases such as organ fibrosis (scleroderma and Dupuytren's Disease), osteoarthritis (impaired articular cartilage repair), and cancer (squamous cell carcinoma and breast cancer)

We use a combination of biochemical, molecular and genetic approaches employing in vitro, in vivo and ex vivo experimental models to study the regulation of distinct TGF-beta signaling pathways, and their cross-talk with other signaling pathways and networks

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Lynne-Marie Postovit

The Postovit lab focuses on cellular plasticity (the ability of a cell to alter phenotype in response to the microenvironment) in cancer. These studies entail understanding how signals from the extracellular space culminate in epigenomic alterations that underpin cancer progression, therapy resistance and metastasis. Matricellular proteins such as CCN1, CCN2 and members of the sFRP family have been shown to orchestrate plasticity, together with stresses such as hypoxia and proteotoxic stress. The lab uses stem cell assays, animal models, sequencing and proteomics together with a systems biology approach to determine how extracellular factors drive plasticity and to target this process in cancers so that therapeutic resistance and/or metastasis can be mitigated.

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Quail DF, Siegers GM, Jewer M and Postovit LM. (2013) Nodal in embryogenesis and tumourigenesis. Int J Biochem Cell Biol 45(4):885–98

David Roberts

The Roberts lab investigates functions of the modulatory extracellular matrix protein thrombospondin-1, its receptors, and downstream signal transduction pathways in cancer. We have identified functions for thrombospondin-1 and its signaling receptor CD47 in regulating tumor angiogenesis, perfusion, and antitumor immunity. CD47 signaling limits recovery of animals from stress, and CD47 expressed by cancer cells and by cells in the tumor microenvironment can limit responses to therapy. Based on these insights, we are developing therapeutics approaches to target CD47 that enhance the efficacy of conventional chemotherapy, radiation therapy, and immunotherapy in murine cancer models.

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Katia Scotlandi

My research work has been focused on pediatric solid tumors particularly bone sarcomas. The goal of my research activity is to contribute to the definition of biomarkers of risk and response that allow more personalized

therapeutic approaches against Ewing sarcoma and osteosarcoma and to pave the way for accelerating the discovery of the most promising biologically and epigenetically-targeted drug. My main achievement is, however, the creation of a research lab specifically devoted to study bone tumors that has obtained worldwide recognition. From 2016 to 2019, I served as Secretary of the WG Sarcoma inside the Italian Alliance against Cancer, the oncologic network of the Italian Ministry of Health, to coordinate preclinical research activities. Not less important, it is my mentoring activity inside the academia. Over the years, I have followed over seventy post-doctoral fellows and junior faculty members, contributing to diffusing knowledge on paediatric oncology

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Peter Siegel

Dr. Siegel's research focuses on the fundamental mechanisms that control organ-selective cancer metastasis. His research interests include migratory and invasive programs that are engaged within cancer cells to promote metastasis. In addition, the interplay between cancer cells and cells within the tumor microenvironment represents a large part of his research program. Finally, the study of metabolic adaptions that accompany cancer metastasis has emerged as a recent area of interest. The Siegel lab employs pre-clinical animal models (both syngeneic and xenograft models) and clinical material (patient-derived xenografts) to identify molecular mediators and cellular processes that promote cancer metastasis to distinct sites (such as the bone, lung, liver and brain).

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Michael J. Soares

Dr. Soares Laboratory investigates specialized survival strategies used by the embryo as it grows within the uterus. Central to the embryo's survival is the formation of the placenta. This organ gains access to the maternal blood supply and facilitates the delivery of nutrients to the fetus. Dr. Soares' Laboratory studies how early stem cells develop into the placenta. They have established in vitro and in vivo model systems for investigating trophoblast cell differentiation and placental development. Through their efforts we have learned that the placenta develops in response to cues present in the maternal environment; and diseases of pregnancy, such as preeclampsia and intrauterine growth restriction, result when the embryo is not successful in its adaptations to the maternal environment. Inadequate in utero adaptive responses have potentially long-lasting impacts on adult health and disease. Thus, an important measure of a healthy placenta is its "plasticity" and capacity to adapt.

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Ulf Smith

Pr. Ulf Smith is a diabetologist and physician. His research is focused on mechanisms for insulin resistance and why obesity drives diabetes development. He has shown that CCN5 is an important regulator of adipogenic cell commitment and a current focus is on cell senescence and its consequences

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Philip Trackman

Dr. Trackman's lab investigates abnormalities in the biosynthesis of the extracellular matrix in pathologies with emphasis on the biology and mechanisms of the multifunctional lysyl oxidase family of proteins. Major attention is paid to mechanisms of promotion and inhibition of oral cancer, and mechanisms of regulation of lysyl oxidase in diabetic bone disease. In addition, the consequence and mechanism of a novel lysyl oxidase mutation on vascular biology is under investigation. Mouse models, in vitro studies, and the use of induced pluripotent stem cells are the primary approaches employed in these collaborative studies.

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Stephen Twigg

As a physician-scientist and educationalist his translational research program since 1995, addressing diabetes acute and chronic complications and related mechanisms, is dedicated to improving clinical outcomes. He has been researching growth factors in diabetes complications. His main expertise is the role played by prosclerotic growth factors, connective tissue growth factor (CTGF/CCN2) and TGF-β in diabetes end-organ complications, with primary focus on liver fibrosis related to diabetes, and wound healing, and diabetic cardiomyopathy, plus diabetic nephropathy. His seminal original scientific research findings to date have been the discovery of a new method by which the insulin-like growth factors circulate in human blood and its molecular basis, that CCN2 mediates high glucose and advanced glycation regulation of matrix turnover and fibrosis in diabetes

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K H Williams, N A Shackel, M D Gorrell, S V McLennan, S M Twigg. (2013) Diabetes and nonalcoholic fatty liver disease: a pathogenic duo Endocr rev.; 34 (1), 84-129

Denys Wheatley

Is a retired academic who has spent more than 40 years researching the cellular and molecular basis of cancer. In several fields, his work has resulted in significant advances; for example, his continuing investigation since 1966 on the primary cilium was proven not just its significance as an almost universal cell organelle, but importantly that its agenesis (lack of development) results in pathological conditions, with now almost 50 disorders being implicated, including neural conditions (1). He has researched protein turnover (the degradation of short and long lived proteins), diffusion theory, intracellular water, arginine deprivation in cancer therapy, the preservation of cells at ambient temperatures (2)

References

Wheatley DN. (2018) The primary cilium – once a "rudimentary" organelle that is now a ubiquitous sensory cellular structure involved in many pathological disorders. J Cell Commun Sign: 12, 211–216. doi: 10.1007/s12079-017-0436-0

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Ralf Weiskirchen

He investigates the molecular mechanisms underlying the pathogenesis of liver disease with particular interest in TGF-β and PDGF signaling. In the past, he established animal models to study hepatic inflammation, fibrosis, cirrhosis, and hepatocellular carcinoma. Moreover, he examines the dynamic role of different CCN proteins in initiation and progression of hepatic disease, their impact on extracellular matrix formation and their contribution to general cellular responses. In addition, he focuses on the identification of novel biomarkers or predispositions for

the assessment of liver disease outcome. The long-term objective of these studies is to translate experimental findings into novel diagnostic or therapeutic strategies. During the last years, he also established laser-ablation-inductively coupled mass spectrometry protocols for measuring and profiling metal concentrations in experimental and clinical samples.

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Zhaolin Yang

My past research was focused on the biogenesis of piRNA, a germ-line specific small non-coding RNAs which function to guard the genome integrity by repressing transposable elements. I have identified multiple novel proteins involved in the piRNA biogenesis, and dissect the molecular mechanisms. We use variety of methodologies ranging from protein biochemistry, cell biology, and animal genetics to computational biology and structural biology. My current research is focused on the epigenetic regulation of cancer, particular acute myeloid leukemia (AML). We harness CRISPR screening to identify novel factors that are required for the AML survival, and study the underlying molecular mechanisms.

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Herman Yeger

My research over the past 40 years centered on the understanding of cell biology in the context of normal development and pathological processes. With reference to the CCN family of genes, work with Prof. B. Perbal (France) reported on the expression of CCN3 in both normal kidney and Wilms tumor. My interest in the CCN family expanded and led to understanding and elaborating their roles in multiple contexts. At SickKids I capitalized on the opportunity to investigate the biology of pediatric cancers, in particular neuroblastoma and, joined with my interest in phytomedicines, we developed a novel therapeutic approach amenable to neuroblastoma, bronchial carcinoids (originating from PNEC) and other cancers. Taken together these initiatives support my research interests in the tumor microenvironment, cell matrix and cell-cell interactions, and therapeutic targeting.

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