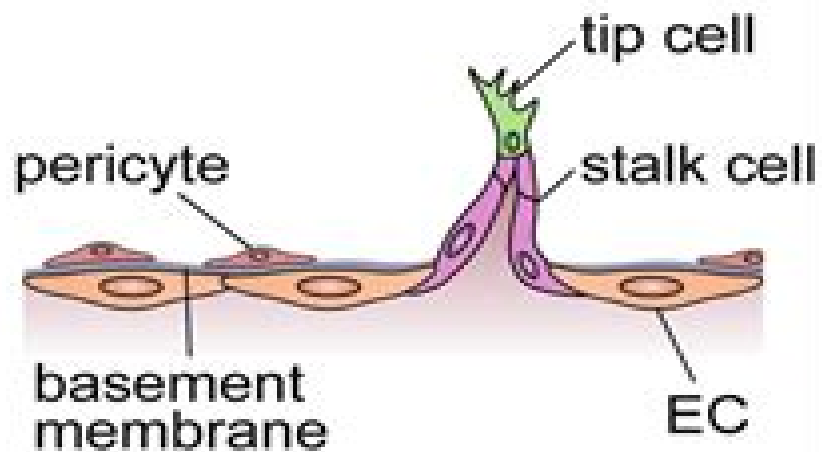
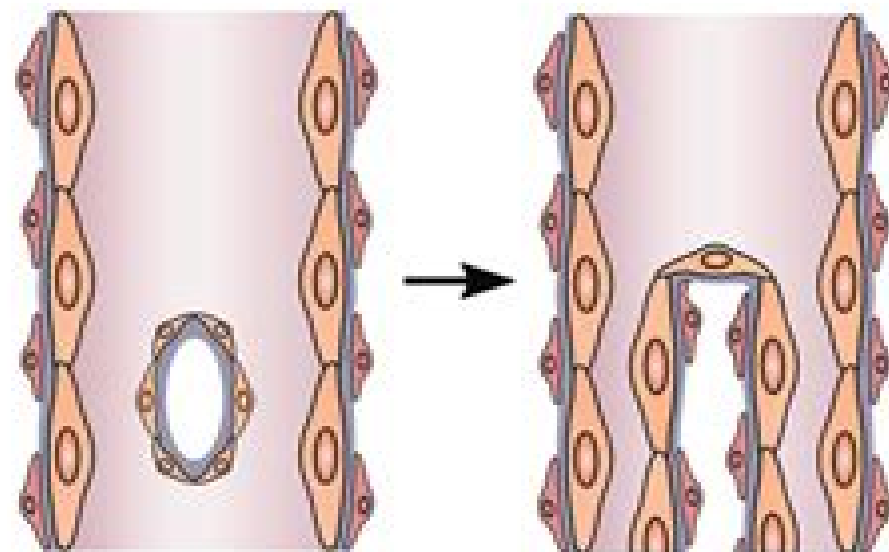


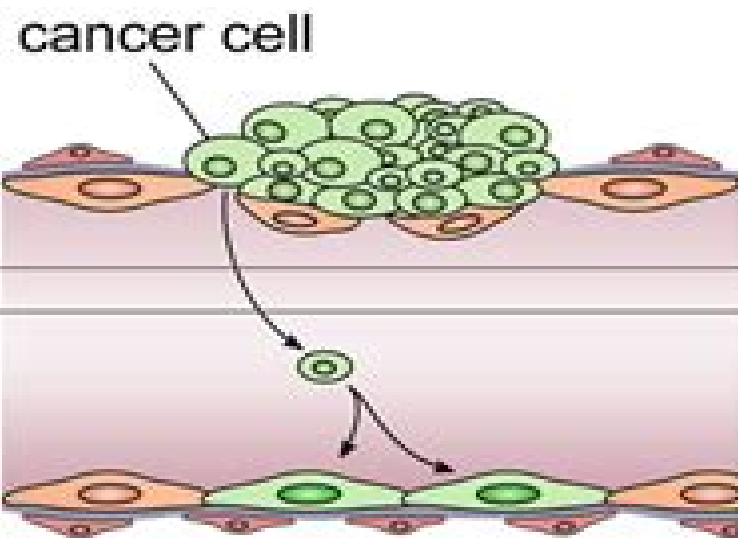
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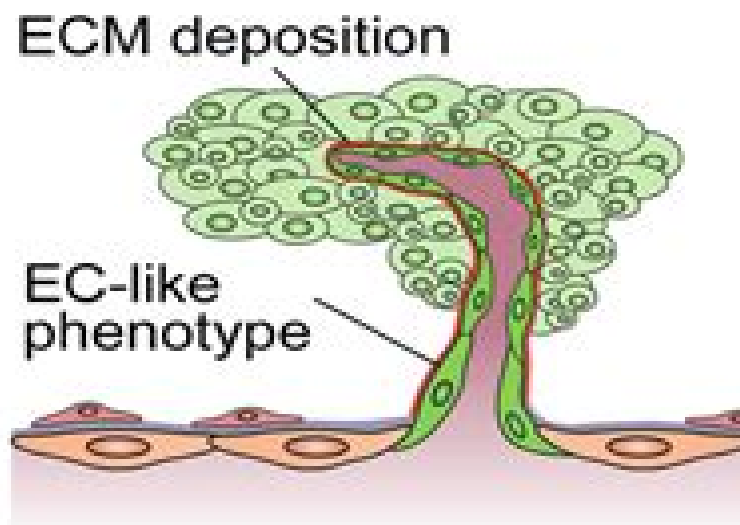


vessel cooption



EC transdifferentiation

vascular mimicry



Angiogenesis In Health And Disease

Gabor M. Rubanyi



Angiogenesis In Health And Disease:

Angiogenesis in Health and Disease June Wade, 2020-09-15 Angiogenesis is the physiological process of the generation of new blood vessels from pre existing vessels that were formed during vasculogenesis By sprouting and splitting angiogenesis perpetuates the growth of the vasculature It is a vital process in growth and development as well as in the formation of granulation tissue and wound healing However it has a major role in the transition of benign tumors into malignant ones Some diseases are characterized by abnormal vasculature Therefore such diseases are combated by inhibiting or inducing the creation of new blood vessels The principle of angiogenesis can be applied clinically in two main areas anti angiogenic therapies and pro angiogenic therapies Anti angiogenic therapies are employed to fight cancer and other malignancies while pro angiogenic therapies are potent against cardiovascular diseases This book includes some of the vital pieces of work being conducted across the world on various topics related to the role of angiogenesis in health and disease It presents the complex subject of angiogenesis in the most comprehensible and easy to understand language It is meant for students who are looking for an elaborate reference text on angiogenesis Angiogenesis in Health, Disease and Malignancy Ali Salajegheh, 2016-03-10 This book is about Angiogenesis A process in which new vasculature is formed from pre existing capillaries Angiogenesis process is associated with the proliferation and growth of both physiologically normal and neoplastic tissues through the formation of vascular supply essential for delivering growth requirements such as oxygen and nutrients The book describes more than 100 genes and their key regulatory functions in the context of normal healthy condition disease and malignancy cancer proliferation and progression New insights into the role of angiogenesis and the therapeutic inhibition of its regulators are investigated due to the great potential for exploitation in the development of a novel treatment for cancer New scientists junior researchers and biomedical science students will find this book an invaluable introductory reference to their insight about angiogenesis and angiogenic role of more than 100 angiogenes and their role in healthy disease and malignant conditions Angiogenesis in Health and Disease Gabor M. Rubanyi, 1999-11-16 Outlines strategies for stimulating capillary formation in hypoxia and ischemia and inhibiting it in cancer diabetes and chronic inflammation This state of the science reference highlights recent progress in the ways to promote formation of new blood vessels in ischemic hypoxic tissue and the means to stifle capillary growth and development in solid tumors diabetic retinopathy and chronic immuno inflammatory disorders such as rheumatoid arthritis and psoriasis Emphasizes practical clinical applications derived from the latest angiogenesis research Written by over 80 leading international experts Angiogenesis in Health and Disease examines new angiogenic regulators such as angiopoietins and TIE receptors describes angiogenic genes such as thymosine B 4 EDG 1 and ARNT proteins analyzes the role of vascular endothelial growth factor VEGF in capillary sprouting investigates behaviors of endogenous agents of angiogenesis including cytokines hormones chemokines and peptide and hematopoietic growth factors explores mechanisms for ameliorating or preventing vascular

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VEGF-mediated vascular functions in health and disease Ziquan Cao, 2015-04-24 Angiogenesis is essential for physiological processes including embryonic development tissue regeneration and reproduction Under various pathological conditions the same angiogenic process contribute to the onset development and progression of many human diseases including cancer diabetic complications ocular disease chronic inflammation and cardiovascular disease Vascular endothelial growth factor VEGF is a key angiogenic factor for physiological and pathological angiogenesis In addition to its strong angiogenic activity VEGF also potently induces vascular permeability often causing tissue edema in various pathological tissues VEGF transduces its vascular signal through two tyrosine kinase receptors VEGFR1 and VEGFR2 the latter being a functional receptor that mediates both angiogenic and vascular permeability effects To study physiological and pathological functions of VEGF we developed novel zebrafish disease models that permit us to study hypoxia induced retinopathy and

cancer metastasis processes We have also administered anti VEGF and anti VEGFR specific antibodies to healthy mice to study the homeostatic role of VEGF in the maintenance of vascular integrity and its functions in various tissues and organs Finally using a zebrafish model we evaluated if VEGF expression is regulated by circadian clock genes In paper I we developed protocols that create hypoxia induced retinopathy in adult zebrafish Adult fli1 EGFP zebrafish were placed in hypoxic water for 3 10 days with retinal neovascularization being analyzed using confocal microscopy This model provides a unique opportunity to kinetically study the development of retinopathy in adult animals using non invasive protocols and to assess the therapeutic efficacy of orally administered anti angiogenic drugs In paper II we developed a zebrafish metastasis model to dissect the complex events of hypoxia induced tumor cell invasion and metastasis in association with angiogenesis at the single cell level In this model fluorescent DiI labeled human or mouse tumor cells were implanted into the perivitelline cavity of 48 hour old zebrafish embryos which were subsequently placed in hypoxic water for 3 days Tumor cell invasion metastasis and pathological angiogenesis were analyzed using fluorescent microscopy in the living fish The average experimental time for this model is 7 days Our protocol offers an opportunity to study molecular mechanisms of hypoxia induced cancer metastasis In paper III we show that systemic delivery of an anti VEGF or an anti VEGF receptor VEGFR 2 neutralizing antibody cause global vascular regression in mice Among all examined tissues the vasculature in endocrine glands intestinal villi and the uterus are most affected in response to VEGF or VEGFR 2 blockades Prolonged anti VEGF treatment resulted in a significant decrease in the circulating levels of the predominant thyroid hormone free thyroxine but not the minimal isoform of triiodothyronine suggesting that chronic anti VEGF treatment impairs thyroid function These findings provide structural and functional bases of anti VEGF specific druginduced side effects in relation to vascular changes in healthy tissues In paper IV we show that disruption of the circadian clock by constant exposure to light coupled with genetic manipulation of key genes in the zebrafish led to impaired developmental angiogenesis A bmal1 specific morpholino inhibited developmental angiogenesis in zebrafish embryos without causing obvious nonvascular phenotypes Conversely a period2 morpholino accelerated angiogenic vessel growth suggesting that Bmal1 and Period2 display opposing angiogenic effects These results offer mechanistic insights into the role of the circadian clock in regulation of developmental angiogenesis and our findings may be reasonably extended to other types of physiological or pathological angiogenesis Overall the results in this thesis provide further insight to angiogenic mechanistic properties in tissues and suggest possible novel therapeutic targets for the treatment of various angiogenesis dependent diseases

Angiogenesis and Vascularisation Józef Dulak, Alicja Józkowicz, Agnieszka Łoboda, 2014-02-10 The book presents the overview of the current knowledge in some fields of vascular biology addressing cellular and molecular aspects of blood vessel formation and their role in health and disease The major factors involved in the formation of blood vessels are presented by scientists actively involved in this area of research Special emphasis is put on the presentation of various molecular mechanisms not addressed

in similar works to date The book is divided into three parts The first part describes the cells and mediators in angiogenesis The significance of various populations of potential endothelial progenitors is particularly highlighted The chapters of the second part focus on molecular mechanisms with special emphasis on the role of hypoxia gasotransmitters and reactive oxygen species as well as microRNAs in regulation of angiogenic processes In the third part the pathological aspects of disturbed aggravated or impaired vascularization are discussed and new modalities for potential therapies are presented The book is intended for scientists and PhD students in the fields of vascular biology and cancer research It may be of interest for medical professionals in the fields of cardiovascular disease diabetes oncology and rheumatoid arthritis

Investigating mechanisms of angiogenesis in health and disease using zebrafish models Zaheer Ali, 2018-12-07

Angiogenesis the growth of blood vessels from an existing vasculature can occur by sprouting from preexisting vessels or by vessel splitting intussusception Pathological angiogenesis drives choroidal neovascularization CNV in age related macular degeneration AMD which is commonly restricted under the retinal pigment epithelium RPE called occult CNV but may also involve vessels penetrating through the RPE into the sub retinal space Pathological vessels are poorly developed insufficiently perfused and highly leaky phenotypes that are considered to drive disease progression and lead to poor prognosis Currently a number of anti angiogenic drugs exists the majority of which target vascular endothelial factor VEGF but although they often are highly beneficial for treating eye diseases in the short term they are generally of limited efficacy in other diseases such as cancer and also have poorer efficacy when used for treatment of eye diseases in the long term A better understanding of the mechanisms underlying pathological angiogenesis can generate new targets for treatment leading to development of better drugs for cancer and retinopathies but perhaps also other angiogenesis dependent diseases in the future In this thesis mechanisms involved in developmental angiogenesis or pathological angiogenesis in the choroid cornea or melanoma was identified These findings highlight the need to further elaborate our knowledge related to angiogenesis in different tissues conditions for a more targeted and potentially effective treatment of diseases in the future In paper I we for the first time identified the choriocapillaries CCs in adult zebrafish and found that occult CNV could be induced by exposing the fish to severe hypoxia Interestingly we found that occult CNV relied on intussusception involving not only de novo generation of intussusceptive pillars but also a previously poorly understood mechanism called pillar splitting This involved HIF VEGF VEGFR2 signaling and evidence that this also occurred in both rats and humans suffering from AMD suggested that the mechanism was conserved and clinically relevant In contrast we found in paper II that the development of CCs in the zebrafish relies on sprouting angiogenesis involve continuous remodeling and delayed maturation of the vasculature in 2D The initial development was found to occur by a unique process of tissue-wide synchronized vasculogenesis As expected VEGFA via VEGFR2 was also critical for the development of these vessels in the zebrafish embryo but surprisingly this was independent on hypoxia inducible factor HIF 1 Inflammatory nuclear factor κ B NF κ B signaling is involved in the progression

of angiogenesis but this signaling pathway has mainly been studied in the inflammatory cells and the role of NF κ B in the endothelial cells during angiogenesis is poorly understood In paper III we found that blocking NF κ B signaling using a specific IKK2 blocker IMD0354 specifically blocks pathological as well as developmental angiogenesis by targeting endothelial cell NF κ B signaling in the endothelial cells Using a rat model for suture induced corneal neovascularization IMD0354 treatment lead to reduced production of inflammatory C C motif chemokine ligand 2 CCL2 C X C motif chemokine ligand 5 CXCL5 and VEGF and thereby reduced pathological corneal angiogenesis in this model Using the zebrafish tumor xenograft model in paper IV we found an association between Microphthalmia associated transcription factor MITF and pigment epithelium derived factor PEDF which was involved in pathological tumor angiogenesis and metastasis Similarly in paper V we used zebrafish transplantation models to study and investigate the use of biocompatible polymers for the delivery of pro angiogenic FGF 2 as a potential treatment strategy for ischemic diseases such as myocardial infarction MI Conclusively this thesis provides new insights into diverse fields of angiogenic assays using zebrafish and reveals new mechanisms of angiogenesis in health and disease This work will hopefully provide a foundation for further studies into occult CNV related to AMD a process that has not been possible to study previously in pre clinical models In addition zebrafish xenograft or other transplantation models used in this work will likely be important to study cancer biology and to develop more attractive pharmaceutical preparations based on biocompatible hydrogels formulated as microspheres in the future

Handbook of Vascular Biology Techniques Mark Slevin,Garry McDowell,2015-03-27 A wide range of research methods for the study of vascular development from basic laboratory protocols to advanced technologies used in clinical practice are covered in this work A range of methodologies such as molecular imaging platforms and signalling analysis along with tumour models are collated here Four sections explore in vitro techniques in vivo and ex vivo manipulations imaging and histological analysis and other novel techniques in vascular biology Readers will discover basic methodologies used for analysis of endothelial cell growth in vitro including co culture models of vessel formation Authors also explore isolation and purification of cells and methods for analysis of data and visualization of localized vasculature with modern imaging platforms Both animal models and human disease are covered in this work Each chapter contains helpful sections on trouble shooting additional notes and links supporting the reader to carry out protocols This book will appeal to students researchers and medical professionals working in all vascular linked fields such as cardio and cerebrovascular cancer and dementia

Humoral Factors in the Regulation of Tissue Growth Piero P. Foa,2012-12-06 Experts in the field of endocrinology as well as ophthalmologists oncologists orthopedists and oral surgeons discuss the nature and mechanism of action of growth stimulating substances whose biological and clinical activities in humans have been demonstrated or are being investigated The monograph represents a good sampler of current basic and applied knowledge in the field

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