

Tissue Barriers: Introducing an exciting new journal

Andrei I Ivanov*

Department of Human and Molecular Genetics; Virginia Institute of Molecular Medicine; VCU Massey Cancer Center; Virginia Commonwealth University; Richmond, VA USA

This Editorial is written to introduce Tissue Barriers, a new Taylor & Francis journal, to the readers of Temperature. It describes the role of temperature in the regulation of different tissue barriers under normal and disease conditions. It also highlights the most interesting articles published in the first volume of Tissue Barriers.

This Editorial introduces Tissue Barriers, a new Taylor & Francis journal, to the readers of Temperature. It has been written for the Special Issue on Temperature and Toxicology because physiological processes in tissue barriers are temperature-dependent and tissue barriers play key roles in the intake and body distribution of xenobiotics. Epithelial and epidermal barriers protect the body from pathogens, xenobiotics and other environmental stresses, and serve to delineate different internal organs with unique cellular architecture and chemical composition.^{1,2} The emergence of vascular barriers and sophisticated blood circulation provided further evolutionary advantage by enabling efficient oxygen and nutrient

transport and a more sophisticated immune defense.³ The pathogenesis of many human diseases involves tissue barrier disruption. A vivid example is inflammation manifested by increased permeability of endothelial and epithelial barriers that results in leukocyte infiltration and tissue edema.^{3,4} Another example is tumor metastasis driven by barrier breaches in solid tumors, thus allowing cancer cells to disseminate and invade different tissues.^{5,6} These examples illustrate the importance of the tissue barrier research field. It is also a rapidly growing field with several thousand papers on the subject published each year.

Permeability of different tissue barriers is regulated by temperature. A notable example of this regulation is the skin, the large barrier that directly senses fluctuations in ambient temperature and has a complex thermoregulatory function.⁷ Modest alterations in skin surface temperature (within 34–40°C) are known to affect epidermal permeability,⁸ while even short heat exposure induces skin barrier breakdown.⁹ The activity of transient receptor potential cation channel, subfamily V, member 4, one of the temperature sensitive cation channels, can regulate epidermal permeability.¹⁰ This channel associates with E-cadherin and therefore may control the assembly and function of intercellular junctions in keratinocytes. Temperature can also affect the function of internal tissue barriers. For example, several studies indicate that ambient temperature dramatically affects the mortality rate in different diseases.^{11–13} This effect could at least partially be mediated by increased permeability of the gut barrier.^{14,15} The most studied example is enhanced intestinal permeability and bacterial translocation during heatstroke.^{14,16} One way of how temperature may affect permeability of tissue barriers is through directing blood flow into different tissue beds. In a warm environment, the skin is

vasodilated; in a cold environment, the skin is vasoconstricted.¹⁷ As a result, more blood is directed to the skin (and less to the viscera) in a warm environment, whereas this relationship reverses in a cold environment. In one of our studies¹⁸ we speculated that skin-to-viscera blood redistribution could contribute to the fact that platelet-activating factor causes hypothermia in a cool environment but fever in a warm environment. The decreased visceral blood flow in a warm environment may contribute to tissue hypoxia in the gut, leading to increased intestinal permeability. The outlined examples illustrate important functional cross-talk between thermoregulation and tissue barriers, although more efforts are required to bring together these exciting areas of research. The expansive diversity of the tissue barrier field somewhat impedes interactions between its different research communities. Thus, there is a communication gap between researchers studying epithelial junctions and their colleagues investigating similar structures in the vascular endothelium. Furthermore, microbiologists examining pathogen interactions with epithelial barriers or bioengineers designing new drug delivery systems are not always aware of recent advances in understanding the fundamental biology and regulation of epithelial junctions.

In a push for bridging interactions between different areas of tissue barrier research, we recently created a new scientific journal, Tissue Barriers. The first volume of Tissue Barriers has been published and is now indexed in PubMed. This Editorial serves to outline our publishing philosophy and highlights some recent Tissue Barriers publications. We publish different types of articles such as Research Papers, Brief Reports, Reviews, Commentaries & Views, and Meeting Reports. Among our most successful accomplishments is several Special Issues of the journal. Two Special Issues dedicated to the

Keywords: adherens junctions, blood flow, cell-cell adhesions, permeability, temperature, tight junctions

© Andrei I Ivanov

*Correspondence to: Andrei I Ivanov;
Email: aivanov2@vcu.edu

Submitted: 10/07/2014

Revised: 10/16/2014

Accepted: 10/16/2014

<http://dx.doi.org/10.4161/23328940.2014.978716>

This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. The moral rights of the named author(s) have been asserted.

claudin protein family and the biology/pathobiology of ductal barriers have already been published, while other Special Issues focusing on tissue barriers in inflammation and epithelial junctions and cancer are currently in preparation.

Our publication portfolio includes papers that can be assigned to any of 4 different categories, as they represent emerging, mainstream, controversial, and underappreciated areas of tissue barrier research. Highlighting emerging areas of tissue barrier research is an important aspect of the general mission of our journal, as reflected by several of our recent publications. For example, we published the first review article that described a novel type of epithelial cell-cell contact, known as tricellular junctions.¹⁹ Furthermore, we highlighted novel signaling pathways that regulate remodeling of epithelial junctions and involve the activity of c-Jun N-terminal kinase²⁰ and protein kinase D.²¹ Other emerging topics have included the functional cross-talk between junctional complexes and adhesive proteins, semaphorins,²² and novel roles of junctional protein cleavage in regulation of epithelial homeostasis.²³

An important goal of our journal is to be on the front line of mainstream directions in tissue barrier research, and to publish on popular and rapidly developing topics. One such topic involves advanced imaging of intercellular junctions. Tissue Barriers has published research papers focusing on live cell imaging and super resolution imaging of adherens and tight junctions in different model epithelia.^{24,25}

We also presented 2 reviews that summarize recent advances in understanding classical signaling pathways that regulate epithelial barriers and involve protein phosphatases²⁶ and small GTPases.²⁷ Finally, several Tissue Barriers papers were dedicated to the structure and functions of the claudin protein family that encompasses major molecular components of epithelial and endothelial tight junctions.²⁸⁻³⁰

Tissue barrier research remains a battlefield of scientific ideas. We reflected on this by publishing papers that target controversial issues in the field. Examples of such controversial issue include the nature and origin of intestinal stem cells,³¹ the roles of

haptoglobin/zonulin proteins in inflammatory bowel diseases,³² and transcriptional versus translational mechanisms of junctional protein downregulation by proinflammatory cytokines.²¹ As for many other extensive research fields, there are some segments of tissue barrier research that are overshadowed by more popular subjects. For example, a lot of attention has been directed at the barrier properties of the gut, skin, and lungs, however the human body contains a number of other important but understudied barriers. Our publication also seeks to highlight the importance of underappreciated tissue barriers. They include ductal barriers on the liver³³ and pancreas,³⁴ as well as the ependymal barrier in the brain ventricular system.³⁵

I believe that these highlighted elements indicate a good start for our new journal. Our confidence with respect to the future success of Tissue Barriers is based on the overwhelmingly positive response received from the research community. Many leading scientists contributed to Tissue Barriers by serving on the Editorial Board, contributing papers, and reviewing submitted manuscripts. We are grateful to all of our colleagues who committed their work and time to Tissue Barriers and we look forward to the future success of our journal.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

- Green KJ, Getsios S, Troyanovsky S, Godsel LM. Intercellular junction assembly, dynamics, and homeostasis. *Cold Spring Harb Perspect Biol* 2010; 2:a000125; PMID:20182611; <http://dx.doi.org/10.1101/cshperspect.a000125>
- Schock F, Perrimon N. Molecular mechanisms of epithelial morphogenesis. *Annu Rev Cell Dev Biol* 2002; 18:463-493; PMID:12142280; <http://dx.doi.org/10.1146/annurev.cellbio.18.022602.131838>
- Komarova Y, Malik AB. Regulation of endothelial permeability via paracellular and transcellular transport pathways. *Annu Rev Physiol* 2010; 72:463-493; PMID:20148685; <http://dx.doi.org/10.1146/annurev-physiol-021909-135833>
- Ivanov AI. Structure and regulation of intestinal epithelial tight junctions: current concepts and unanswered questions. *Adv Exp Med Biol* 2012; 763:132-148; PMID:23397622
- Ivanov AI, Naydenov NG. Dynamics and regulation of epithelial adherens junctions: recent discoveries and controversies. *Int Rev Cell Mol Biol* 2013; 303:27-99; PMID:23445808; <http://dx.doi.org/10.1016/B978-0-12-407697-6.00002-7>

- Savagner P. Leaving the neighborhood: molecular mechanisms involved during epithelial-mesenchymal transition. *Bioessays* 2001; 23:912-923; PMID:11598958; <http://dx.doi.org/10.1002/bies.1132>
- Romanovsky A. Skin temperature: its role in thermoregulation. *Acta Physiol* 2014; 210:498-507; <http://dx.doi.org/10.1111/apha.12231>
- Denda M, Sokabe T, Fukumi-Tominaga T, Tominaga M. Effects of skin surface temperature on epidermal permeability barrier homeostasis. *J Invest Dermatol* 2007; 127:654-659; PMID:17068482; <http://dx.doi.org/10.1038/sj.jid.5700590>
- Park JH, Lee JW, Kim YC, Prausnitz MR. The effect of heat on skin permeability. *Int J Pharmaceut* 2008; 359:94-103; <http://dx.doi.org/10.1016/j.ijpharm.2008.03.032>
- Sokabe T, Tominaga M. The TRPV4 cation channel: A molecule linking skin temperature and barrier function. *Commun Integr Biol* 2010; 3:619-621; PMID:21331258; <http://dx.doi.org/10.4161/cib.3.6.13461>
- Kokolus KM, Capitano ML, Lee CT, Eng JW, Waight JD, Hylander BL, Sexton S, Hong CC, Gordon CJ, Abrams SI, Repasky EA. Baseline tumor growth and immune control in laboratory mice are significantly influenced by subthermoneutral housing temperature. *Proc Natl Acad Sci U S A* 2013; 110:20176-20181; PMID:24248371; <http://dx.doi.org/10.1073/pnas.1304291110>
- Liu E, Lewis K, Al-Saffar H, Krall CM, Singh A, Kulchitsky VA, Corrigan JJ, Simons CT, Petersen SR, Musteata FM, Bakshi CS, Romanovsky AA, Sellati TJ, Steiner AA. Naturally occurring hypothermia is more advantageous than fever in severe forms of lipopolysaccharide- and Escherichia coli-induced systemic inflammation. *Am J Physiol Reg Integr Comp Physiol* 2012; 302:R1372-1383; <http://dx.doi.org/10.1152/ajpregu.00023.2012>
- Romanovsky AA, Shido O, Sakurada S, Sugimoto N, Nagasaka T. Endotoxin shock-associated hypothermia. How and why does it occur?. *Ann N Y Acad Sci* 1997; 813:733-737; PMID:9100963; <http://dx.doi.org/10.1111/j.1749-6632.1997.tb51775.x>
- Costa KA, Soares AD, Wanner SP, Santos R, Fernandes SO, Martins Fdos S, Nicoli JR, Coimbra CC, Cardoso VN. L-arginine supplementation prevents increases in intestinal permeability and bacterial translocation in male Swiss mice subjected to physical exercise under environmental heat stress. *J Nutr* 2014; 144:218-223; PMID:24259555
- Dokladny K, Moseley PL, Ma TY. Physiologically relevant increase in temperature causes an increase in intestinal epithelial tight junction permeability. *Am J Physiol Gastrointest Liver Physiol* 2006; 290:G204-212; PMID:16407590; <http://dx.doi.org/10.1152/ajpgi.00401.2005>
- Lambert GP. Stress-induced gastrointestinal barrier dysfunction and its inflammatory effects. *J Animal Sci* 2009; 87:E101-108; <http://dx.doi.org/10.2527/jas.2008-1339>
- Romanovsky AA, Ivanov AI, Shimansky YP. Selected contribution: ambient temperature for experiments in rats: a new method for determining the zone of thermal neutrality. *J Appl Physiol* 2002; 92:2667-2679; PMID:12015388
- Ivanov AI, Patel S, Kulchitsky VA, Romanovsky AA. Platelet-activating factor: a previously unrecognized mediator of fever. *J Physiol* 2003; 553:221-228; PMID:14565987; <http://dx.doi.org/10.1113/jphysiol.2003.055616>
- Furuse M, Izumi Y, Oda Y, Higashi T, Iwamoto N. Molecular organization of tricellular tight junctions. *Tissue barriers* 2014; 2:e28960; PMID:25097825; <http://dx.doi.org/10.4161/tisb.28960>
- You H, Lei P, Andreadis ST. JNK is a novel regulator of intercellular adhesion. *Tissue barriers* 2013; 1:e26845; PMID:24868495; <http://dx.doi.org/10.4161/tisb.26845>
- Naydenov NG, Baranwal S, Khan S, Feygin A, Gupta P, Ivanov AI. Novel mechanism of cytokine-induced

- disruption of epithelial barriers: Janus kinase and protein kinase D-dependent downregulation of junction protein expression. *Tissue barriers* 2013; 1:e25231; PMID:24665409; <http://dx.doi.org/10.4161/tisb.25231>
22. Treps L, Le Guelte A, Gavard J. Emerging roles of Semaphorins in the regulation of epithelial and endothelial junctions. *Tissue barriers* 2013; 1:e23272; PMID:24665374; <http://dx.doi.org/10.4161/tisb.23272>
 23. Nava P, Kamekura R, Nusrat A. Cleavage of transmembrane junction proteins and their role in regulating epithelial homeostasis. *Tissue barriers* 2013; 1:e24783; PMID:24665393; <http://dx.doi.org/10.4161/tisb.24783>
 24. Indra I, Troyanovsky R, Troyanovsky SM. Afadin controls cadherin cluster stability using clathrin-independent mechanism. *Tissue barriers* 2014; 2:e28687; PMID:25045601; <http://dx.doi.org/10.4161/tisb.28687>
 25. Twiss F, Oldenkamp M, Hiemstra A, Zhou H, Mathéron L, Mohammed S, de Rooij J. HGF signaling regulates Claudin-3 dynamics through its C-terminal tyrosine residues. *Tissue barriers* 2013; 1:e27425; PMID:24665413; <http://dx.doi.org/10.4161/tisb.27425>
 26. McCole DF. Phosphatase regulation of intercellular junctions. *Tissue barriers* 2013; 1:e26713; PMID:24868494; <http://dx.doi.org/10.4161/tisb.26713>
 27. Citalan-Madrid AF, Garcia-Ponce A, Vargas-Robles H, Betanzos A, Schnoor M. Small GTPases of the Ras superfamily regulate intestinal epithelial homeostasis and barrier function via common and unique mechanisms. *Tissue barriers* 2013; 1:e26938; PMID:24868497; <http://dx.doi.org/10.4161/tisb.26938>
 28. Koval M. Differential pathways of claudin oligomerization and integration into tight junctions. *Tissue barriers* 2013; 1:e24518; PMID:24665398; <http://dx.doi.org/10.4161/tisb.24518>
 29. Lu Z, Ding L, Lu Q, Chen YH. Claudins in intestines: Distribution and functional significance in health and diseases. *Tissue barriers* 2013; 1:e24978; PMID:24478939; <http://dx.doi.org/10.4161/tisb.24978>
 30. Van Itallie CM, Anderson JM. Claudin interactions in and out of the tight junction. *Tissue barriers* 2013; 1:e25247; PMID:24665401; <http://dx.doi.org/10.4161/tisb.25247>
 31. De Mey JR, Freund JN. Understanding epithelial homeostasis in the intestine: An old battlefield of ideas. recent breakthroughs and remaining controversies. *Tissue barriers* 2013; 1:e24965; PMID:24665395; <http://dx.doi.org/10.4161/tisb.24965>
 32. Vanuytsel T, Vermeire S, Cleynen I. The role of Haptoglobin and its related protein, Zonulin, in inflammatory bowel disease. *Tissue barriers* 2013; 1:e27321; PMID:24868498; <http://dx.doi.org/10.4161/tisb.27321>
 33. Rao RK, Samak G. Bile duct epithelial tight junctions and barrier function. *Tissue barriers* 2013; 1:e25718; PMID:24665411; <http://dx.doi.org/10.4161/tisb.25718>
 34. Kojima T, Yamaguchi H, Ito T, Kyuno D, Kono T, Konno T, Sawada N. Tight junctions in human pancreatic duct epithelial cells. *Tissue barriers* 2013; 1:e24894; PMID:24665406; <http://dx.doi.org/10.4161/tisb.24894>
 35. Jimenez AJ, Dominguez-Pinos MD, Guerra MM, Fernandez-Llebrez P, Perez-Figares JM. Structure and function of the ependymal barrier and diseases associated with ependyma disruption. *Tissue barriers* 2014; 2:e28426; PMID:25045600; <http://dx.doi.org/10.4161/tisb.28426>