Pathology Perspectives on the Applications of Complex In Vitro Models in Pharmaceutical Research and Development

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EMPLOYMENT

2017 – Present Global Pathology Team Leader, Pfizer Inc, Cambridge, MA

2014-2017 Research Fellow, Exploratory Drug Safety, Pfizer Inc, Andover, MA

2010-2014 Associate Research Fellow, Pfizer Inc, Cambridge, MA

2007-2010 Principal Veterinary Pathologist, **Clinical Pathology Dept**, Bristol-Myers Squibb (BMS), New Brunswick, New Jersey

2004-2007 Senior Veterinary Pathologist, Pathology/Clinical Pathology Dept., BMS, New Brunswick, New Jersey

2001-2004 Veterinary Pathologist, Pathology Dept., BMS, New Brunswick, New Jersey

EDUCATION

1998 Doctor of Veterinary Science, University of Guelph, Guelph, Canada

1995 Doctor of Veterinary Medicine, University of Guelph, Guelph, Canada

OTHER CREDENTIALS

Board certification in Anatomic and Clinical Pathology and Toxicology

Cochair of the ESTP/STP Complex In Vitro Model Working Subgroup (2020-present)

American Society for Veterinary Clinical Pathology (ASVCP, 2004-present): Immediate Past President (2017-2018), President (2016-2017), President-elect (2015-2016), Chair of the Regulatory Affairs Committee (RAC, 2011-2013), RAC member (2008-2010, 2014-2015) and

chair, Pre-Meeting Workshop, The 2011 Guide to Toxicologic Clinical Pathology, Nashville, TN (Dec 2011), Development Committee (2007-2008)
Society of Toxicologic Pathology (STP, 2002-present): Executive Committee (2019-2023), Scientific and Regulatory Policy Committee (SRPC) Sage (2015-2016), Chair (2014-2015), Cochair (2013-2014), Member (2012-2013)
American College of Veterinary Pathology (ACVP, 2000-present): ACVP Governance Task Force and Examination Committee (2018-2019), ACVP Annual Meeting Clinical Pathology Sessions Chair (2016), Focused Scientific Session Coordinator and Abstracts Editor for Veterinary Pathology (2009- 2010), Awards Chair and Specialty Group Co-Coordinator (2007- 2008), Education Committee (2007-2010), Toxicologic Pathology Committee Chair (2006) and Member (2005, 2007)

SUMMARY OF MPS RESEARCH CONTRIBUTIONS

Baran SW, Brown PC, Baudy AR, Fitzpatrick SC, Frantz C, Fullerton A, Gan J, Hardwick RN, Hillgren KM, Kopec AK, Liras JL, Mendrick DL, Nagao R, Proctor WR, Ramsden D, Ribeiro AJS, Stresser D, Sung KE, Sura R, Tetsuka K, **Tomlinson L**, Van Vleet T, Wagoner MP, Wang Q, Arslan SY, Yoder G, Ekert JE. Perspectives on the evaluation and adoption of complex in vitro models in drug development: Workshop with the FDA and the pharmaceutical industry (IQ MPS Affiliate). ALTEX - Alternatives to animal experimentation. 2022, doi: 10.14573/altex.2112203.

Hollingshead BD, **Tomlinson L**, Finley J, Doshna C, Ritenour C, Barricklow J, Oppenheimer SR, O'Neil SP, Moore JL, Patterson NH, Nicholson SP, Norris JL, Caprioli RM, Beaumont, K, King-Ahmad AJ, Vispute S, Cook JC, Radi Z and Schuler M. An orthogonal methods assessment of topical drug concentrations in skin and the impact for risk assessment in the viable epidermis. Regul Toxicol Pharmacol. 2021,123, 104934.

Rogers MT, Gard AL, Gaibler R, Mulhern TJ, Strelnikov R, Azizgolshani H, Cain BP, Isenberg BC, Haroutunian NJ, Raustad NE, Keegan PM, Lech MP, **Tomlinson L**, Borenstein JT, Charest JL, Williams C. A high-throughput microfluidic bilayer co-culture platform to study endothelial-pericyte interactions. Sci Rep. 2021 Jun 9;11(1):12225.

Kopec AK, Yokokawa R, Khan N, Horii I, Finley JE, Bono CP, Donovan C, Roy J, Harney J, Burdick AD, Jessen B, Lu S, Collinge M, Sadeghian RB, Derzi M, **Tomlinson L**, Burkhardt JE. Microphysiological systems in early stage drug development: Perspectives on current applications and future impact. J Toxicol Sci. 2021;46(3):99-114.

Schuler M, **Tomlinson L**, Homiski M, Cheung J, Zhan Y, Coffing S, Engel M, Rubitski E, Seitis G, Hales K, Robertson A, Vispute S, Cook J, Radi Z, Hollingshead B. Experiments in the EpiDerm 3D Skin In Vitro Model and Minipigs In Vivo Indicate Comparatively Lower In Vivo Skin Sensitivity of Topically Applied Aneugenic Compounds. Toxicol Sci. 2021 Feb 26;180(1):103-121.

PRESENTATION ABSTRACT

Extensive efforts are ongoing to build relevant complex in vitro models (CIVM) in order to reduce animal usage in drug development worldwide. There is great potential in this field but several challenges still exist before pharmaceutical companies can incorporate these models routinely in development pipelines. Joint proceedings published from the 2020 Food & Drug Administration (FDA) and Innovation and Quality Microphysiological Systems (IQ MPS) Affiliate workshop are instructive on how CIVM are currently being used by pharmaceutical companies and how the FDA and industry can work together to evolve the advancement of qualifying models for a specific context of use. The FDA has enabled this evolution further with the pilot ISTAND program. These efforts build upon the longstanding efforts of ©Organisation for Economic Co-operation and Development (OECD) resulting in guidelines driving utilization of the reconstructed epidermis and corneal epithelium models to evaluate cosmetics for skin (corrosion, irritation, phototoxicity) and ocular irritation, respectively. The OECD guidelines are the result of extensive validation and have been adopted over the last 18 years and are a guidepost to how risk assessment can evolve to support the reduction, refinement, and replacement (3Rs) alternatives for the use of animals in research, testing, and education. What is still needed, is an understanding between regulators and pharmaceutical companies on how to manage the standardization of CIVM to support broader usage.

There is a wide range of platforms evolving, making it difficult to proceed with a single one. Understanding which platforms can most efficiently and effectively answer efficacy, safety, and/or regulatory needs is a work in progress. There are many examples of scientific achievement that are bringing us closer to that goal and a few of those will be described. The collaborative efforts of pathologists/scientists/engineers to overcome challenges and find the most physiologically relevant solutions are considered key and will be highlighted. Cross company, professional society and consortia efforts will be needed to move CIVM into the future and will be reviewed. Considerations for adoption of the different platforms must recognize differences in needs across the disciplines of ADME (absorption, distribution, metabolism, and excretion), pharmacology, and safety assessment; the qualifications for context of use are dependent on the scientific question being asked and the intended use of the data obtained. Finally, the promise and utility of CIVM contingent upon the focus of scientific communities to overcome the obstacles of submission by pharmaceutical companies and acceptance by regulators worldwide will be described.