

Sipes NS, Martin MT, Kothiya P, Reif DM, Judson R, Richard A, Houck KA, Dix DJ, Kavlock RJ and **Knudsen** TB (2013) Profiling 976 ToxCast chemicals across 331 enzymatic and receptor signaling assays *Chem Res Toxicol* 26: 878-895.

Green ML, Pisano MM, Prough RL and **Knudsen** TB (2013) Release of targeted p53 from the mitochondrion as an early signal during mitochondrial dysfunction. *Cell Signaling* 25: 2383-2390.

Rotroff DM, Houck KA, **Knudsen** TB, Sipes NS, Martin MT, Reif DM, Abassi Y, Jin C, Stampfl M and Judson RS (2013) Using Real-Time Growth Kinetics to Measure Hormone Mimicry for 1816 Unique ToxCast Chemicals using T47D Human Ductal Carcinoma Cells. *Chem Res Toxicol* 26: 1097-1107.

Wambaugh JF, Reif D, Gangwal S, Mitchell-Blackwood J, Arnot J, Joliet O, Judson R, **Knudsen** T, Egeghy P, Rabinowitz J, Vallero D, Setzer RW, and Cohen-Hubal E (2013) Simulation of environmental chemical fate for exposure prioritization in the ExpoCast project. *Env Sci & Technol* 47: 8479-8488.

Judson R, Kavlock R, Martin M, Reif D, Houck K, **Knudsen** T, Richard A, Tice R, Whelan M, Xia M, Huang R, Austin C, Daston G, Hartung T, Fowle J, Wooge W, Tong W, and Dix D. (2013) Perspectives on validation of high-throughput pathway-based assays supporting the 21st Century toxicity testing vision. A*LTEX* 30: 51-66.

Hao R, Bondesson M, Singh AV, **Knudsen** TB, Gorelick DA and Gustafsson J-A (2013) Distinct sets of genes, but similar biological pathways, are regulated by estrogen during zebrafish development. *PLoS ONE* 8(11): e79020. doi:10.1371/journal.pone.0079020.

Kleinstreuer N, Yang J, Berg E, **Knudsen** T, Richard A, Martin M, Reif D, Judson R, Polokoff M, Kavlock R, Dix D and Houck K (2014) Phenotypic screening of the ToxCast chemical library to classify toxic and therapeutic mechanisms. *Nature Biotech* 32: 583-591.

Rotroff D, Matthew M, Dix D, Filer D, Houck K, **Knudsen** T, Sipes N, Reif D, Menghang X, Huang R, and Judson R (2014) Predictive endocrine testing in the 21st century using in vitro assays of estrogen receptor signaling responses. *Environ Sci Technol* 48: 8706-8716.

Tal TL, McCollum CW, Harris PS, Olin J, Kleinstreuer N, Wood CE, Hans C, Shah S, Merchant FA III, Bondesson M, **Knudsen** TB, Padilla S and Hemmer MJ (2014) Immediate and long-term consequences of vascular toxicity during zebrafish development. *Reprod Toxicol* 48: 51-61.

deWoskin RS, Shah I and **Knudsen** TB (2014) Virtual Models (vM) in Toxicology. Encyclopedia of Toxicology, 3rd Edition (P Wexler, Editor), 4896 pages. Elsevier, inc. pp 948-957.

Judson R, Houck K, Martin M, **Knudsen** T, Thomas RS, Sipes N, Shah I, Wambaugh J and Crofton K (2014) In Vitro and Modeling Approaches to Risk Assessment from the U.S. Environmental Protection Agency ToxCast Program. *Basic & Clin Pharmacol Toxicol* 115: 69-76.

Krewski D, Andersen M, Boekelheide K, Bois F, Burgoon L, Chiu W, DeVito M, El-Masri H, Flowers L, Goldsmith M, Hattis D, Knight D, **Knudsen** T, Lefew W, Paoli G, Perkins E, Rusyn I, Tan C, Teuschler L, Thomas R, Whelan M, Zacharewski T, Zeise L, and Cote I (2014) Advanced Approaches to Recurring Issues in Risk Assessment. In: "Next Generation Risk Assessment: Incorporation of Recent Advances in Molecular, Computational, and Systems Biology. Final Report." EPA/600/R-14/004. pp 94-110.

Knudsen TB, Keller DA, Sander M, Carney EW, Doerrer NG, Eaton DL, Fitzpatrick SC, Hastings KL, Mendrick DL, Tice RR, Watkins PB and Whelan M (2014) FutureTox II: In vitro data and in silico models for predictive toxicology. *Toxicol Sci* (in press).





Scholarly Activities:

An important goal in birth defects research is to derive the architecture and function of developing systems as biological networks. At the Birth Defects Center, Dr. Knudsen's laboratory used genomic and systems biology to understand the developmental consequences of prenatal exposures to alcohol and environmental toxicants. With vast genomics data and bioinformatics tools now at hand, efforts are underway to reverse-engineer gene regulatory networks (GRNs) that underlie birth defects and developmental abnormalities. Dr. Knudsen relocated to the National Center for Computational Toxicology at the US Environmental Protection Agency in late 2007 to spear-head a new research program aiming to develop a sophisticated computer model of a mammalian embryo that can be used to help scientists better understand the prenatal risks posed by chemicals and other environmental stressors the 'Virtual Embryo Project' (v-Embryo™). This project is using computers to develop models of GRNs and reconstruct embryonic tissues in silico (http://www.epa.gov/ncct/v-Embryo/). 'Virtual tissue' technology enables researchers to interact with a computer-simulated environment of specific embryonic tissues. The ability to perform complex operations on simulated system gives insight to conditions hard to evaluate due to time, scale, and cost (monetary and animal). Challenges for technology development include a knowledgebase to extract, organize, and store data (database) and facts (literature) about the tissue in a computable form, and a simulation engine for multi-scale models to study how different mechanisms interact at one level and cause effects at a higher level. Validated computational (in silico) models of the embryo may someday help scientists integrate in vitro data at different scales molecules to phenotype as well as to help link toxicity pathways with prenatal developmental effects in vivo.



Barrier M, Chandler K, Jeffay S, Hoopes M, **Knudsen** T and Hunter S (2012) Mouse Embryonic Stem Cell Adherent Cell Differentiation and Cytotoxicity (ACDC) assay. Chapter, Springer Protocols (Humana Press) Methods in Molecular Biology – Developmental Toxicology (Eds: J Hansen and C Harris). Vol 889, pp 181-195.

Kavlock R, Chandler K, Dix D, Houck K, Hunter S, Judson R, Kleinstreuer N, **Knudsen** T, Martin M, Padilla S, Reif D, Richard A, Rotroff D and Sipes N (2012) Update on EPA's ToxCast program: providing high throughput decision support tools for chemical risk management. *Chemical Res Toxicol*. 25: 1287-1302.

Knudsen T, Martin M, Chandler K, Kleinstreuer N, Judson R and Sipes N (2012) Predictive Models and Computational Toxicology. In: Teratogenicity Testing: Methods and Protocols. Edited: P Barrow, Humana Press, New York. Chapter 26, pp 343-374.

Rotroff DM, Dix DJ, Houck KA, **Knudsen** TB, Martin MT, McLaurin KL, Reif DM, Crofton KM, Singh AV, Xia M, Huang R and Judson RS (2012) Using in vitro high-throughput screening assays to identify potential endocrine disrupting chemicals. *Environ Hlth Persp.* 121: 7-14.

Luijten M, Singh AV, Bastian CD, Verhoef A, Westerman A, Pisano MM, Schipper MA, Dollé ME, Verhoef A, Green ML, Piersma AH, de Vries A, Green ML and **Knudsen** TB (2012) Lasting effects on body weight and mammary gland gene expression in female mice upon early life exposure to n-3 but not n-6 high-fat diets *PLoS One* 8(2):e55603. doi: 10.1371/journal.pone.0055603.

Solecki R Barbellion S, Bergmann B, Bürgin H, Buschmann J, Clark R, Comotto L, Fuchs A, Faqi A, Gerspach , R, Grote K, Hakansson H, Hofmann T, Hübel U, Inazaki TH, Khalil S, **Knudsen** TB, Lingk W, Kudicke S, Makris S, Müller S, Paumgartten F, Roma EM, Schneider S, Shiota K, Tamborini E, Tegelenbosch M,Tiramani M, Ulbrich B, van Duijnhoven EAJ, Wise D and Chahoud I (2013) Harmonization of description and classification of fetal observations: Achievements and still standing problems. *Reprod Toxicol.* 35: 48-55.

Kleinstreuer NC, Dix DJ, Houck KA, Kavlock RJ, **Knudsen** TB, Martin MT, Reif DM, Crofton KM, Hamilton K, Hunter R, Paul KB, Shah I and Judson RS (2013) In vitro perturbation of cancer hallmark processes is associated with rodent chemical carcinogenesis. *Toxicol Sci.* 131: 40-55.

Kleinstreuer N, Dix D, Rountree M, Baker N, Sipes N, Reif D, Spencer R, and **Knudsen** T (2013) A computational model predicting disruption of blood vessel development. *PLoS Comput Biol* 9(4): e1002996. doi:10.1371/journal.pcbi.1002996.

Allard P, Kleinstreuer N, **Knudsen** T and Colaiácovo MP (2013) A novel chemical screening strategy for assessing environmental germline disruption in C. elegans. *Env Hlth Persp* 121: 717-724.