Isabel Lea, Ph.D.

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CONTACT INFORMATION

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PROFESSIONAL PROFILE

Dr. Isabel Lea is a toxicologist in ToxStrategies' Health Sciences practice. She has more than 20 years of experience, focusing on evaluating and assessing data for environmental chemicals with the potential to cause health effects. Dr. Lea has broad experience, ranging from conducting primary research and performing systematic literature reviews to translating large bodies of evidence in scientific databases. Having conducted more than 50 literature reviews, she routinely develops search strategies and inclusion/exclusion criteria, extracts evidence from heterogeneous study types, conducts critical appraisals for study quality, and synthesizes evidence to develop qualitative conclusions. Dr. Lea has used this expertise to developing documents regarding risk-based toxicity assessment for regulatory agencies. She was involved in the preparation of OSRI (Other Significantly Relevant Information) reports identified for Endocrine Disruptor Screening Program Tier 1 screening, for use in their weight-of-evidence assessments for Tier 2 testing.

Dr. Lea has specific expertise in performing literature reviews to collect and synthesize data describing genetic alterations associated with the development of cancerous lesions, highlighted by a review of point mutations, insertions, deletions, and loss of heterozygosity, which documented the acquisition of alterations in tumor suppressor genes and oncogenes that could induce or promote the development of malignancy. This work was then used as the basis to design a structured query language (SQL) database and a public website platform (Genetic Alterations in Cancer knowledge system) that allowed users to query, search, and download data. Dr. Lea's role covered all aspects of the project—in addition to conducting the literature reviews, she also led an evaluation team and developed project-specific instructions, data dictionaries, and quality control criteria that led to the development of a genetic alterations database and website. In addition, Dr. Lea has significant experience evaluating *in vivo* and *in vitro* data, including genetic toxicology (Comet, micronucleus, and Ames assays), toxicogenomics, and high-throughput screening (Tox21) and high-content screening data. This work was conducted in support of toxicology projects for the National Toxicology Program (NTP) and the NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM).

Dr. Lea has extensive experience with toxicology data management for the Chemical Effects in Biological Systems (CEBS) and Integrated Chemical Environment (ICE) platforms. For CEBS, she played key roles, as lead data scientist and Program Manager. The CEBS database contains data from the NTP Toxicology Testing Program. In this capacity, Dr. Lea developed standard processes for data input to the CEBS system, created verification and validation processes to ensure that public data accurately represented the data delivered to the system. She was instrumental in promoting standard terminology in CEBS and oversaw the addition of CEBS terms to the Ontology for Biomedical Investigation. Promoting the FAIR guiding principles, she also was instrumental in making CEBS data available through Healthdata.gov. Regarding her role with ICE, which provides curated data sets and tools designed to facilitate the safety assessment of chemicals, Dr. Lea played a key role in updating data sets to include cancer endpoints.

Dr. Lea has published academic and professional work in peer-reviewed journals, has reviewed submissions for scientific journals, and regularly attends and presents at professional conferences and colloquia. Dr. Lea is a Program Manager Professional (PMP), which has provided her with the knowledge, expertise, and skill needed to lead a large team of scientists and manage simultaneous projects while delivering on time, within budget, and with excellent client satisfaction ratings.

EDUCATION, DEGREES, AND CERTIFICATIONS

Ph.D., Molecular and Cell Biology
London University and the Zoological Society of London, UK

B.S. Microbiology
London University, London, UK

P.M.P. Project Management Professional (2019)
Project Management Institute

SELECTED PROFESSIONAL EXPERIENCE

Toxicology

Performed systematic reviews of the cancer literature to collect and synthesize data describing genetic alterations, such as point mutations, insertions, deletions, and loss of heterozygosity in tumor suppressor genes and oncogenes.

Described site- and exposure-specific patterns in genetic pathways and mutation profiles for human respiratory-tract cancers associated with tobacco use.

Described genetic alterations in 9000 colorectal tumors, showing that point mutations in codon 248 of the TP53 gene occurred approximately three times more frequently in carcinomas than adenomas.

Composed chapter on Electrolytes, Blood Gases and Acid-Base Balance for Clinical Chemistry of the Laboratory Animal (https://doi.org/10.1201/9781315155807).

Prepared four OSRI (Other Significantly Relevant Information) reports for four chemicals identified for Endocrine Disruptor Screening Program Tier 1 screening for use in their weight-of-evidence assessments for determination of Tier 2 testing.

Data Science

Managed NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) Integrated Chemical Environment (ICE) database in support of the development of alternative test methods. Integrated *in vivo*, *in vitro*, and *in silico* data from quantitative structure-activity relationship (QSAR) and *in vitro*–to–*in vivo* extrapolation (IVIVE) modeling. Established the use of controlled vocabularies to facilitate data selection and improve the user experience for ICE users.

Led team and performed a key role in the redesign and management of NTP's toxicological testing database (CEBS), working with NTP to develop standard data import procedures, perform statistical analysis of data, and develop standardized reports for *in vivo* and *in vitro* data, single- and multigenerational studies, and multiple endpoints. Developed workflows to analyze multi-well plate data and a website to allow users to interact with the data.

Collected, cleansed, and provided depositor feedback for structured and unstructured toxicological testing data. Work included managing the development process and reporting progress to the client and recommending design strategies based on knowledge of the data and the development environment. Monitored the functionality and performance of client products.

Developed the NTP's Genetic Alterations in Cancer (GAC) database, collating genetic mutations in malignant lesions.

Project Management

Managed, expanded, and delivered a program handling a portfolio of up to 10 projects and developing services simultaneously. Allocated and scheduled resources while leading a multidisciplinary team comprising direct employees and subcontractors.

Monitored staff and provided comprehensive oversight of scientific team efforts, and guided development of reports and other written work products, including manuscripts for publication, CMMI level 3 documentation and processes, and software performance quality documents.

MANUSCRIPTS

Borghoff SJ, Cohen SS, Jiang X, **Lea IA**, Klaren WD, Chappell GA, Britt JK, Rivera BN, Choksi NY, Wikoff DS. 2023. Updated systematic assessment of human, animal and mechanistic evidence demonstrates lack of human carcinogenicity with consumption of aspartame. Food Chem Toxicol 172:113549, online ahead of print.

Lea IA, Pham LL, Antonijevic T, Thompson C, Borghoff SJ. 2022. Assessment of the applicability of the threshold of toxicological concern for per- and polyfluoroalkyl substances. Regul Toxicol Pharmacol 133:105190, open access.

Lea IA, Chappell GA, Wikoff DS. 2021. Overall lack of genotoxic activity among five common low- and no-calorie sweeteners: A contemporary review of the collective evidence. Mutat Res Genet Toxicol Environ Mutagen 868–869:503389. doi: 10.1016/j.mrgentox.2021.503389. PMID: 34454695.

Gentry R, Greene T, Chappell G, **Lea I**, Borghoff S, Yang C, Rathman J, Ribeiro JV, Hobocienski B, Mostrag A, Rodricks J, Clewell H. 2021. Integration of evidence to evaluate the potential for neurobehavioral effects following exposure to USFDA-approved food colors. Food Chem Toxicol 151:112097. doi: 10.1016/j.fct.2021.112097. Epub 2021 Mar 4. PMID: 33677041.

Gentry R, Rodricks J, Clewell H, Greene T, Chappell G, **Lea I**, Borghoff S, Yang C, Rathman J, Ribeiro JV, Hobocienski B, Mostrag A. 2021. RE: Response to the Office of Environmental Health Hazard Assessment on comments related to Gentry et al. (2021). Food Chem Toxicol 152:112202. doi: 10.1016/j.fct.2021.112202. Epub 2021 Apr 17. PMID: 33872725.

Palermo CM, Foreman JE, Wikoff DS, **Lea I**. 2021. Development of a putative adverse outcome pathway network for male rat reproductive tract abnormalities with specific considerations for the androgen sensitive window of development. Curr Res Toxicol 22:2:254–271. doi: 10.1016/j.crtox.2021.07.002. PMID: 34401750; PMCID: PMC8350458.

Bell S, Abedini J, Ceger P, Chang X, Cook B, Karmaus AL, **Lea I**, Mansouri K, Phillips J, McAfee E, Rai R, Rooney J, Sprankle C, Tandon A, Allen D, Casey W, Kleinstreuer N. 2020. An integrated chemical environment with tools for chemical safety testing. Toxicol in Vitro 67:104916. https://doi.org/10.1016/j.tiv.2020.104916.

Lea IA, Borghoff S, Travlos GS. 2018. Electrolytes, blood gases and acid-base balance. In: Kurtz DM, Travlos GS (eds): The Clinical Chemistry of Laboratory Animals (3rd edition). CRC Press, Boca Raton, FL.

Jackson MA, Yang L, **Lea I**, Rashid A, Kuo B, Williams A, Lyn Yauk C, Fostel J. 2017. The TGx-28 65 biomarker online application for analysis of transcriptomics data to identify DNA damage-inducing chemicals in human cell cultures. Environ Mol Mutagen 58(7):529–535.

Lea IA, Gong H, Paleja A, Rashid, A, Foster J. 2017. CEBS: A comprehensive annotated database of toxicological data. Nucleic Acids Res 45(D1):D964–D971.

Bhusari S, Malarkey DE, Hong HH, Wang Y, Masinde T, Nolan M, Hooth NJ, **Lea IA**, Vasconcelos D, Sills RC, Hoenerhoff MJ. 2014. Mutation spectra of Kras and Tp53 in urethral and lung neoplasms in B6C3F1 mice treated with 3,3′,4,4′-tetrachloroazobenzene. Toxicol Pathol 42(3):555–564.

Waters MD, Jackson MA, **Lea IA**. 2010. Characterizing and predicting carcinogenicity and mode-of-action using conventional and toxicogenomics methods. Mutat Res 705(3):184–200.

Lea IA, Jackson MA, Dunnick JK. 2009. Genetic pathways to colorectal cancer. Mutat Res 670(1–2):96–98.

Lea IA, Jackson MA, Li X, Bailey S, Peddada SD, Dunnick JK. 2007. Genetic pathways and mutation profiles of human cancers: Site- and exposure-specific patterns. Carcinogenesis 28:1851–1858.

Jackson MA, **Lea I**, Rashid A, Peddada SD, Dunnick JK. 2006. Genetic alterations in cancer knowledge system: Analysis of gene mutations in mouse and human liver and lung tumors. Toxicol Sci 90:400–418.

Lea IA, Widgren EE, O'Rand MG. 2004. Association of sperm protein 17 with A-kinase anchoring protein 3 in flagella. Reprod Biol Endocrinol 2:57.

Lea IA, Widgren EE, O'Rand MG. 2002. Analysis of recombinant mouse zona pellucida protein 2 (ZP2) constructs for immunocontraception. Vaccine 20(11–12):1515–1523.

Lea IA, Sivashanmugam P, O'Rand MG. 2001. Zonadhesin: characterization, localization, and zona pellucida binding. Biol Reprod 65(6):1691–700.

Lea IA, van Lierop MJ, Widgren EE, Grootenhuis A, Wen Y, van Duin M, O'Rand MG. 1998. A chimeric sperm peptide induces antibodies and strain-specific reversible infertility in mice. Biol Reprod 59(3):527–536.

Lea IA, Kurth B, O'Rand MG. 1998. Immune response to immunization with sperm antigens in the macaque oviduct. Biol Reprod 58(3):794–800.

O'Rand MG, **Lea IA**. 1997. Designing an effective immunocontraceptive. J Reprod Immunol 36(1–2):51–59; Review.

Adoyo PA, **Lea IA**, Richardson RT, Widgren EE, O'Rand MG. 1997. Sequence and characterization of the sperm protein Sp17 from the baboon. Mol Reprod Dev 47(1):66–71.

Lea IA, Adoyo P, O'Rand MG. 1997. Autoimmunogenicity of the human sperm protein Sp17 in vasectomized men and identification of linear B cell epitopes. Fertil Steril 67(2):355–361.

Lea IA, Richardson RT, Widgren EE, O'Rand MG. 1996. Cloning and sequencing of cDNAs encoding the human sperm protein, Sp17. Biochim Biophys Acta 1307(3):263–266.

Lea I, Moore HD, Latchman DS. 1991. Differential expression of the mouse U1a and U1b SnRNA genes is not dependent on sequence differences in the octamer motif. Biochem J 277(Pt 3):719–722.

ABSTRACTS AND PRESENTATIONS

Lea IA, Feifarek D, Mihalchik A, Heintz M, Haws L, Nyambego H, Goyak K, Borghoff SJ. Evaluation of the endocrine disrupting potential of di-isodecyl phthalate. Abstract 3930, Society of Toxicology Annual Meeting, Salt Lake City, UT, March 2024.

Borghoff SJ, Feifarek D, Mihalchik A, Heintz M, Haws L, Nyambego H, Goyak K, **Lea IA**. Evaluation of the endocrine disrupting potential of di-isodecyl phthalate. Abstract 3931, Society of Toxicology Annual Meeting, Salt Lake City, UT, March 2024.

Lynn SG, **Lea IA**, Urban J, Borghoff SJ, Wikoff D, Fitch S, Perry C, Choksi N, Britt J, Heintz M, Klaren W, et al. Development and application of systematic approach to inventory and interrogate thyroid hormone network information. Abstract 4357, Society of Toxicology Annual Meeting, Salt Lake City, UT, March 2024.

Lea IA, Heintz MM, Feifarek D, Haws LC, Borghoff SJ. Weight-of-evidence evaluation of endocrine activity for di-isodecyl phthalate (DIDP) and di-isononyl phthalate (DINP). Poster presented at Society of Toxicology Annual Meeting, Nashville, TN, March 2023.

Mihalchik AL, Choksi NY, **Lea I**, Wood ML. Modern strategies to evaluate drug impurities. Session presented at Society of Toxicology Annual Meeting, Nashville, TN, March 2023.

Wikoff D, Edwards S, Angrish M, Baumgartner, Bever R, Borghoff S, Chappell G, Chew R, Fitch S, Hench G, Hamernik K, Henderson D, Kirk A, **Lea I**, Mandel M, Payne L, Shapiro S, Urban J, Williams D, Markey K. Application of systematic methods to characterize thyroid adverse outcome pathways (AOPs). Presented at 10th annual meeting of American Society for Cellular and Computational Toxicology (virtual), October 2021.

Bell S, Mansouri K, Phillips J, Chang X, Abedini J, Karmaus AL, **Lea I**, Rai R, Allen DG, Casey W, Kleinstreuer NC. NCEATM computational tools and resources supporting alternative test method development and evaluation. Presented at the 59th Annual Meeting of Society of Toxicology, Anaheim CA, March 2020. Abstract #2976-P607.

Sheridan E, Moose J, Liu Y, Martini C, **Lea I**, Fostel J. NTP high-level summary data collections in the Chemical Effects in Biological Systems (CEBS) database. Presented at the 15th International Congress of Toxicology, Honolulu, HI, July 2019. Poster PS01-0606.

Bhawana B, **Lea I**, Liu Y, Martini C, Fostel J. Access to National Toxicology Program histopathology lesion collection in Chemical Effects in Biological Systems (CEBS) database. Presented at the 38th Annual Symposium of Society for Toxicologic Pathology, Raleigh, NC, June 2019. Poster P040.

Lea I, Liu Y, Sheridan E, Motti D, Martini C, Fostel J, Auerbach S. Hallmark gene set annotation for NTP toxicogenomic studies. Presented at the 58th Annual Meeting of Society of Toxicology, Baltimore, MD, March 2019. Abstract #1743-P119.

Martini C, Liu Y, Motti D, Johnson J, McCormick K, **Lea I**, Fostel F. Integrating assay datasets into Chemical Effects in Biological Systems (CEBS). Presented at the 58th Annual Meeting of Society of Toxicology, Baltimore, MD, March 2019. Abstract #1749-P125.

Sheridan ER, Jackson M, Paleja A, Martini C, Rashid A, **Lea I**, Fostel J. Improved searching in the Chemical Effects in Biological Systems (CEBS) database leads to greater utility of NTP data. Presented at the 57th Annual Meeting of Society of Toxicology, San Antonio, TX, March 2018. Abstract 2525-P887.

Sheridan E, Raghuraman A, Brown P, Jackson M, Martini C, **Lea I**, Smith-Roe S, Witt K, Fostel J. Genetic toxicology data in the Chemical Effects in Biological Systems (CEBS) database. Presented at the 48th Annual Meeting of Environmental Mutagenesis and Genomics Society, San Antonio, TX, September 2018. Poster P3.

Lea I, Yang L, Rashid A, Fostel JM. Chemical Effects in Biological Systems (CEBS) Database: Treatment-related findings. Presented at the 56th Annual Meeting of Society of Toxicology, Baltimore, MD, March 2017. Abstract 2918-P412.

Martini C, Rashid A, Paleja A, **Lea I**, Fostel JM. Chemical Effects in Biological Systems (CEBS) database: Treatment-related findings. Presented at the 56th Annual Meeting of Society of Toxicology, Baltimore, MD, March 2017. Abstract 1381-P119.

Sheridan E, Martini C, Shaw M, Shockley K, Brix A, Rashid A, **Lea I**, Fostel J. Using the Chemical Effects in Biological Systems (CEBS) database to answer pathology questions. Presented at the 36th Annual Symposium of Society for Toxicologic Pathology, Montreal, Quebec, Canada, June 2017. Poster P035.

Jackson M, Yang L, Yauk CL, **Lea I**, Kuo B, Williams A, Rashid A, Fostel J. The TGx-28.65 biomarker — A web-based application using transcriptomics to identify DNA damage-inducing chemicals. Presented at the 48th Annual Meeting of Environmental Mutagenesis and Genomics Society, Raleigh, NC, September 2017. Abstract 1224.

Lea I, Rashid A, Favaro C, Fostel J. Chemical Effects in Biological Systems (CEBS) database: Advanced histopathology search applications. Presented at the 54th Annual Meeting of Society of Toxicology, San Diego, CA, March 2015. Abstract 2195-P410.