Karen H. Dingley, Ph.D.

SENIOR CONSULTANT

CONTACT INFORMATION

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PROFESSIONAL PROFILE

Dr. Karen Dingley is a Senior Consultant in ToxStrategies' Pharmaceuticals Practice. She has more than 20 years experience in the pharmaceutical arena and previously directed efforts on the use of drug metabolism and pharmacokinetics (DMPK) at several leading pharmaceutical companies. This work included representing DMPK on cross-functional teams, as well as preparing project strategies and development plans, overseeing study design and data interpretation, working with contract research organizations (CROs), and collaborating to design and interpret PK/PD and efficacy studies. Dr. Dingley's experience ranges from providing preclinical absorption, distribution, metabolism, and excretion (ADME) support to contributing to regulatory documents and filing investigational new drug applications (INDs). She is proficient in managing interdisciplinary projects involving chemists, biologists and clinicians.

Dr. Dingley has significant experience in authoring and critically reviewing source reports, INDs, clinical protocols, investigator brochures and briefing books to support clinical trials. She is well versed in the regulations that govern the use of human and animal subjects in research. Dr. Dingley is also experienced in performing human PK and dose predictions to support first-in-human (FIH) clinical trials, and in assessing drug-drug interaction potential.

EDUCATION AND DEGREES EARNED

1995 Doctor of Philosophy (Ph.D.)
University of York, United Kingdom

1988 Bachelor of Science (B.Sc.), Biochemistry
University College of Swansea, United Kingdom

PROFESSIONAL HONORS/AWARDS

2013 Pro Bono award from New Jersey Section of the American Chemical Society for service to Drug Metabolism Group

PROFESSIONAL ASSOCIATIONS

2010-2017 New Jersey Drug Metabolism Discussion Group. New Jersey Section of the American Chemical Society. Steering Committee member.

SELECTED PROFESSIONAL EXPERIENCE

As Director of DMPK at a leading pharmaceutical company, oversaw internal and outsourced drug metabolism and PK activities on multiple projects. This work included study design, data interpretation and report generation. Wrote and critically reviewed submission documents, including source reports, INDs, investigator brochures and supporting materials for clinical trials. Helped to guide department strategy.

In leadership positions at other pharmaceutical companies, acted as the DMPK project representative on multiple internal and partnered programs. Worked with CROs to design and perform *in vitro* and *in vivo* ADME studies. Collaborated with software development scientists on new ADME-prediction tools. Assisted in formulating and executing project strategies. Gained experience in drug formulation on a 6-month rotation to a pharmaceuticals department.

Served for three years as the chair of a departmental training committee. Collaborated on the design, development, and implementation of cross functional training and career development opportunities for approximately 360 employees.

As a Senior Biomedical Scientist at a U.S. national laboratory, was principal investigator in the Molecular Toxicology Group, and applied analytical techniques in ADME, pharmacokinetic, and genetic toxicology studies in humans and laboratory animals. Developed and managed collaborations with academic research institutions and pharmaceutical companies in the US and Europe. Additionally, served as Deputy Chairperson on the lab's review board for human subject research and was also a member of the Institutional Animal Care and Use Committee (IACUC)

SKILLS AND TRAINING

- Training in pharmacokinetics, PK-PD modeling, and WinNonlin software
- Additional training courses taken in Metabolism of Drugs, Reaction Mechanisms, Transporters in Drug Discovery and Development, Enzyme Kinetics, Inhibition, and Scientific Writing

SELECTED MANUSCRIPTS

Lagiakos HR, Zou Y, Igawa H, Therrien E, Lawrenz M, Kato M, Svensson M, Gray F, Jensen K, Dahlgren M, Pelletier R, **Dingley K,** et al. 2025. *In silico* enabled discovery of KAI-11101, a preclinical DLK inhibitor for the treatment of neurodegenerative disease and neuronal injury. J Med Chem 68(3):2720-2741.

Xue Y, Wang L, Huo R, Chen M, Melo B, **Dingley K**, et al. 2024. 1β-Hydroxydeoxycholic acid as an endogenous biomarker in human plasma for assessment of CYP3A clinical drug-drug interaction potential. Drug Metab Dispos 52(9):966–974.

Lawrenz M, Svensson M, Kato M, **Dingley K**, et al. 2023. A computational physics-based approach to predict unbound brain-to-plasma partition coefficient, Kp,uu. Chem Inf Model 63(12):3786–3798.

Tsvetkov L, Pittsenbarger J, Atsriku C, Devine P, **Dingley K**, et al. 2022. Inhibition of CDC7 with Sgr-2921 in AML models results in enhanced DNA damage and anti-leukemic activity as monotherapy and in combination with standard of care agents. Blood 140(Supp 1):5961–5962.

Yin W, Nie Z, **Dingley K**, et al. 2021. Characterization of potent paracaspase MALT1 inhibitors for hematological malignancies. Blood 138(Supp 1):1187.

Liu W, Hussain Z, Zang Y, Sweis RF, Romero FA, Finke PE, … **Dingley KH**, et al. 2018. Optimization of preclinical metabolism for somatostatin receptor subtype 5-selective antagonists. ACS Med Chem Lett (9):1088–1093.

Powles MA, Galgoci A, Misura A, Colwell L, **Dingley K**, Tang W, et al. 2018. *In vivo* efficacy of relebactam (MK-7655) in combination with imipenem/cilastatin in murine infection models. Antimicrob Agents Chemother 62:e02577–17.

Harper BH, Wang L, Zhu C, Kar NF, Li B, Moyes CR, … **Dingley K**, et al. 2017. Investigation of piperazine benzamides as human β3 adrenergic receptor agonists for the treatment of overactive bladder. Bioorg Med Chem Lett 27(4):1094–1098.

Wang Y, Villalta PW, Peng L, **Dingley KH**, Malfatti MA, Turteltaub KW, Turesky RJ. 2017. Mass spectrometric characterization of an acid-labile adduct formed with 2-amino-1-methyl-phenylimidazo[4,5-b]pyridine and albumin in humans. Chem Res Toxicol 30(2):705–714.

Zhu C, Wang L, Zhu Y, Guo ZZ, Liu P, Hu Z, … **Dingley KH**, et al. 2017. Discovery of phenyl acetamides as potent and selective GPR119 agonists. Bioorg Med Chem Lett 27(5):1124–1128.

Edmondson SD, Zhu C, Kar NF, Di Salvo J, Nagabukuro H, Sacre-Salem B, **Dingley K**, et al. 2016. Discovery of vibegron: A potent and selective beta 3 adrenergic receptor agonist for the treatment of overactive bladder. J Med Chem 59(2):609–623.

Guo L, Parker DL, Zang Y, Sweis RF, Liu W, Sherer EC, … **Dingley KH**, et al. 2016. Discovery and optimization of a novel triazole series of GPR142 agonists for the treatment of type 2 diabetes. ACS Med Chem Lett 7(12):1107–1111.

Wilson JE, Kurukulasuriya R, Sinz C, Matthew Lombardo, Kate Bender, Dann Parker, … **Dingley K**, et al. 2016. Discovery and development of benzo-[1,2,4]-triazolo-[1,4]-oxazepine GPR142 agonists for the treatment of diabetes. Bioorg Med Chem Lett 26(12):2947–2951.

Zhu C, Kar NF, Li B, Costa M, **Dingley KH**, Di Salvo J, et al. 2016. Discovery of benzamides as potent human β3 adrenergic receptor agonists. Bioorg Med Chem Lett 26(1):55–59.

Liu P, Hu Z, DuBois BG, Moyes CR, Hunter DN, Zhu C, … **Dingley KH**, et al. 2015. Design of potent and orally active GPR119 agonists for the treatment of type II diabetes. ACS Med Chem Lett 6(8):936–941.

Dingley KH, Ubick EA, Vogel JS, Ognibene TJ, Malfatti MA, Kulp K, Haack KW. 2014. DNA isolation and sample preparation for quantification of adduct levels by accelerator mass spectrometry. Methods Mol Biol 1105:147–157.

Moyes CR, Berger R, Goble SD, Harper B, Shen DM, Wang L, … **Dingley KH**, et al. 2014. Design, synthesis, and evaluation of conformationally restricted acetanilides as potent and selective β3 adrenergic receptor agonists for the treatment of overactive bladder. J Med Chem 57(4):1437–1453.

Borowsky AD, **Dingley KH**, Ubick E, Turteltaub KW, Cardiff RD, Devere-White R. 2006. Inflammation and atrophy precede prostatic neoplasia in a PhIP-induced rat model. Neoplasia 8(9):708–715.

Degregorio MW, **Dingley KH**, Wurz GT, Ubick E, Turteltaub KW. 2006. Accelerator mass spectrometry allows for cellular quantification of doxorubicin at femtomolar concentrations. Cancer Chemother Pharmacol 57(3):335-342.

Malfatti MA, **Dingley KH**, Nowell-Kadlubar S, Ubick EA, Mulakken N, Nelson D, Lang NP, et al. 2006. The urinary metabolite profile of the dietary carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine is predictive of colon DNA adducts after a low-dose exposure in humans. Cancer Res 66(21):10541–10547.

Tompkins EM, Farmer PB, Lamb JH, Jukes R, **Dingley K**, Ubick E, et al. 2006. A novel 14C-postlabeling assay using accelerator mass spectrometry for the detection of O6-methyldeoxy-guanosine adducts. Rapid Commun Mass Spectrom 20(5):883–891.

Brown K, **Dingley KH**, Turteltaub KW. 2005. Accelerator mass spectrometry for biomedical research. Meth Enzymol 402:423–443.

Ebeler SE, **Dingley KH**, Ubick E, Abel S, Mitchell AE, Burns SA, et al. 2005. Animal models and analytical approaches for understanding the relationships between wine and cancer. Drugs Exp Clin Res 31(1):19–27.

Rickert DE, **Dingley K**, Ubick E, Dix KJ, Molina L. 2005. Determination of the tissue distribution and excretion by accelerator mass spectrometry of the nonadecapeptide 14C-Moli1901 in beagle dogs after intratracheal instillation. Chem Biol Interact 155(1–2):55–61.

Chepanoske CL, Brown K, Turteltaub KW, **Dingley KH**. 2004. Characterization of a peptide adduct formed by *N*-acetoxy-2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP), a reactive intermediate of the food carcinogen PhIP. Food Chem Toxicol 42(8):1367–1372.

Cupid BC, Lightfoot TJ, Russell D, Gant SJ, Turner PC, **Dingley KH**, et al. 2004. The formation of AFB(1)-macromolecular adducts in rats and humans at dietary levels of exposure. Food Chem Toxicol 42(4):559–569.

Mally A, Zepnik H, Wanek P, Eder E, **Dingley K**, Ihmels H., et al. 2004. Ochratoxin A: Lack of formation of covalent DNA adducts. Chem ResToxicol 17(2):234–242.

Dingley KH, Ubick EA, Chiarappa-Zucca ML, Nowell S, Abel S, Ebeler SE, et al. 2003. Effect of dietary constituents with chemopreventive potential on adduct formation of a low-dose of the heterocyclic amines PhIP and IQ and phase II hepatic enzymes. Nutr Cancer 46(2):212–221.

Martin EA, Gaskell M, Al-Azzawi F, Garner RC, Brown K, Boocock DJ, Mattock E, Pring DW, **Dingley K**, et al. 2003. Tamoxifen DNA damage detected in human endometrium using the ultra sensitive technique of accelerator mass spectrometry. Cancer Res 63(23):8461–8465.

Turesky RJ, Richoz J, Constable A, Curtis KD, **Dingley KH**, Turteltaub KW. 2003. The effects of coffee on enzymes involved in metabolism of the dietary carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine in rats. Chem-Biol Interact 145(3):251–265.

Love AH, Hunt JR, Roberts ML, Southon JR, Chiarappa-Zucca ML, **Dingley KH**. 2002. Use of tritium accelerator mass spectrometry for tree ring analysis. Environ Sci Technol 36(13):2848–2852.

Williams KE, Carver TA, Miranda JJ, Kautiainen A, Vogel JS, **Dingley K**, et al. 2002. Attomole detection of in vivo protein targets of benzene in mice: Evidence for a highly reactive metabolite. Mol Cell Proteomics 1(11):885–895.

ABSTRACTS AND PRESENTATIONS

Burnett J, Sychterz C, Zhu D, Shakeel F, **Dingley K**, Chen W, et al. Prospective application of physiologically based pharmacokinetic (PBPK) modeling to inform the design of a clinical drug-drug Interaction (DDI) study: Case study of mezigdomide. Poster presented at American Society of Clinical Pharmacology and Therapeutics (ASCPT) Annual Meeting, Colorado Springs, CO, March 2024.

Ramírez-Valle F, Adams M, Beebe L, Chen J, Chuaqui C, Connarn JN, Corin AF, **Dingley KH**, et al. A novel MK2 inhibitor for the treatment of ankylosing spondylitis and other inflammatory diseases. Abstract 1536, Annual Meeting of the American College of Rheumatology Conference, Atlanta, GA, November 2019.