Ling Liu, Ph.D., DABT

MANAGING SCIENTIST

CONTACT INFORMATION

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PROFESSIONAL PROFILE

Dr. Ling Liu is Managing Scientist in ToxStrategies' Pharmaceuticals/Biopharmaceuticals Practice. She is a board-certified toxicologist with 20 years of toxicology and drug discovery experience in the pharmaceutical industry, with both large pharmaceutical companies and small start-ups. She has nonclinical experience with biologic, small-molecule products, and gene therapy in a wide variety of therapeutic indications, including neurology, muscular dystrophy, oncology, metabolic disease, and rare diseases, as well as multiple routes of administration (oral, intravenous, subcutaneous, intracerebroventricular).

She has experience as a project-team liaison on multidisciplinary discovery and development project teams, responsible for developing and implementing the nonclinical safety strategy to support nonclinical development of pipeline assets, and writing regulatory submissions (pre-INDs, INDs, IBs, briefing books) and due diligence evaluations.

Dr. Liu also specializes in directing and monitoring both non-GLP and GLP toxicity studies, as well as more complex gene therapy studies. She has expertise in protocol development, design, conduct, data interpretation, and reporting of nonclinical toxicity studies in mice, rats, rabbits, dogs, and nonhuman primates. With a background in developmental biology and pharmacology, Dr. Liu understands target pathways, underlying biological mechanisms of disease states, and the biological mechanisms of toxicity.

Prior to joining ToxStrategies, Dr. Liu worked as a toxicologist in the pharmaceutical industry and as a pharmacologist for a start-up company.

EDUCATION AND DEGREES EARNED

Certificate	Principles and Practices of Gene Therapy (Stanford University, 2020)
Certificate	Clinical Trials Design and Management (University of California, San Diego, 2019)
DABT	Diplomate, American Board of Toxicology (2007–present)
Ph.D.	Developmental Biology, Stockholm University, Sweden
M.S.	Zoological Ecology, East China Normal University, Shanghai, P.R. China
B.S.	Biology, East China Normal University, Shanghai, P.R. China

PROFESSIONAL MEMBERSHIPS

American College of Toxicology

Society of Toxicology

SELECTED PROFESSIONAL EXPERIENCE

Study Director

Served as single point of control for exploratory toxicity studies. Responsible for protocol development, design, conduct, data interpretation, and reporting of nonclinical toxicity studies.

Led evaluation of chemical entities, biologics, and gene therapy, including studies in mice, rats, rabbits, dogs, and nonhuman primates.

Responsible for protocol development, design, conduct, data interpretation, and reporting of exploratory and mechanistic studies to support selection of lead molecules and regulatory submissions.

Study Monitor

Responsible for scientific oversight of outsourced studies, from protocol development through issuance of final report. Studies included *in vitro* assay, *in vivo* toxicity, and gene therapy studies.

Partnered with the CRO-SD and CRO study team to ensure that work was conducted to corporate expectations.

Performed all regulatory responsibilities in compliance with applicable regulatory standards, ensuring compliance with applicable SOPs and guidelines, and Animal Use Protocols.

Drug Safety Evaluator/Team Lead

Responsible for developing and implementing the nonclinical safety strategy for projects, from idea to IND-directed toxicology studies, for the development of selected molecules. Ensured alignment of safety strategies with overall objectives of the therapeutic area. Served as a scientific subject-matter expert (SME) in collaboration with regulatory strategy leads on dossier preparation and responses to regulatory queries.

Assessed potential safety concerns and reviewed current knowledge of specific targets of interest. Functioned as the primary author of the safety sections of TKRs to provide an integrated assessment of potential safety issues and a proposed target risk minimization strategy.

Represented drug safety positions on several projects; responsible for data interpretation and developing nonclinical safety strategies—including go/no-go decision making—along with writing and reviewing regulatory documents.

Early discovery toxicology:

- Developed non-GLP toxicology capabilities for acute tolerability and repeat-dose evaluation. Led exploratory and mechanistic *in vivo* toxicology studies (non-GLP) in rodents. Designed, executed, and reported *in vivo* studies to support discovery and development projects. Managed a team of technicians performing *in vivo* studies.
- Acted as study monitor for outsourced studies in support of development programs.
- Performed the duties of a Drug Safety Evaluation Representative on discovery and development project teams.
- Led non-GLP toxicological evaluation of lead compounds for diabetes program. Designed and executed non-GLP toxicological studies. Contributed to lead molecule FDA pre-IND briefing books.

Preclinical pharmacology:

- Served as lead pharmacologist on a diabetes program. Established glucose clamp capability for the characterization of clinical candidates in diabetes programs and demonstrated the mechanism of action underlying target inhibition to acute and chronic changes in glucose homeostasis. Employed the use of glucose clamp for pharmacological evaluation and selection of viable backup compounds.
- Pharmacologically validated DPP4 as a target for type 2 diabetes. Demonstrated temporal mechanistic links underlying DPP4 inhibition to acute and chronic changes in glucose homeostasis and insulin resistance.
- Designed and executed preclinical PK/PD studies to analyze PK parameters, and to understand PK/PD relationships.
- Responsible for identification, pharmacology/safety evaluation, and selection of viable backup compounds.

In a forward-genetics study of anxiety disorder, led the central nervous system program for a major pharmaceutical firm:

- Established behavioral screen platforms for the identification of mutant mice with anxiety-related behaviors and ataxic phenotypes.
- Pharmacologically validated anxiety screen platforms with pharmacological agents for target validation and evaluation of novel compounds for anxiety.
- Analyzed ataxic mice generated by chemical mutagen (ENU) mutagenesis.
- Co-investigator of SBIR grant: “Animal models for drug development in anxiety.”

Doctoral and Post-Doctoral Work

Generated mouse models of human ataxia using ENU (N-ethyl N-nitrosourea, mutagen) forward (phenotype based) genetic screens to identify and study a phenotype of interest.

Analyzed gene expression profile in calcium channel mutants with Affymetrix chip technology.

Cloned the gene mutated in meander-tail mice. Meander-tail mutant mice have an autosomal recessive mutation that results in a kinky tail and ataxic gait.

Cloned mouse a-sarcoglycan gene and studied its expression and distribution during myogenesis *in vivo* and *in vitro*.

Discovered a novel e-sarcoglycan-containing complex in skeletal muscle and studied its association and expression during myogenesis.

Established a mouse model of human limb-girdle muscular dystrophy by generation of a-sarcoglycan null mice.

Generated laminin a2 transgenic mice under the control of a P0 promoter, aiming to correct the phenotypes of mice with laminin a2-deficiency in their peripheral nerves.

MANUSCRIPTS

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Guo LT, Zhang X, Kuang W, Xu H, **Liu LA**, Vilquin J-T, et al. (2003) Laminin a2 deficiency and muscular dystrophy; genotype-phenotype correlation in mutant mice. Neuromuscul Disord 13:207–215.

Dressman D, Araishi K, Imamura M, Sasaoka T, **Liu LA**, Engvall E, Hoffman EP. 2002. Delivery of a- and b-sarcoglycan by recombinant adeno- associated virus: Efficient rescue of muscle, but differential toxicity. Hum Gene Ther 13:1631–1646.

Bergman RL, Inzana KD, Monroe WE, Shell LG, **Liu LA**, Engvall E, Shelton GD. 2002. Dystrophin-deficient muscular dystrophy in a labrador retriever. J Am Anim Hosp Assoc 38:255–261.

O'Brien DP, Johnson GC, **Liu L**, Guo LT, Engvall E, Powell HE, Shelton GD. 2001. Laminin a 2 (merosin)-deficient muscular dystrophy and demyelinating neuropathy in two cats. J Neurol Sci 189:37–43.

Shelton GD, **Liu L**, Guo LT, Smith GK, Christiansen JS, Thomas WB, et al. 2001. Muscular dystrophy in female dogs. J Vet Intern Med 15(3):240–244.

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Liu L, Engvall E. 1999. Sarcoglycan isoforms in skeletal muscle. J Biol Chem 274(53):38171–38176.

Kuang W, Xu H, Vachon HP, **Liu L**, Loechel F, Wewer UM, Engvall E. 1998. Merosin-deficient congenital muscular dystrophy; partial genetic correction in two mouse models. J Clin Invest 102(4):844–852.

Pierre HV, Xu H, **Liu L**, Loechel F, Hayashi Y, Arahata K, et al. 1997. Integrins (a7b1D) in muscle function and survival; disrupted expression in merosin-deficient congenital muscular dystrophy. J Clin Invest 100(7):1870–1881.

Liu L, Vachon HP, Kuang W, Xu H, Kylsten P, Engvall E. 1997. Adhalin, a marker of myogenic differentiation; up-regulation during myotube formation and associated re-localization from cytoplasm to sarcolemma. Biochem Biophys Res Commun 235(1):227–235.