Dr. Frank C. Richardson, DVM, PhD, DABT

Principal Toxicologist

Executive Summary:

Experienced pharmaceutical development professional with progressive large pharmaceutical and biotechnology experience in: toxicologic assessment of drug candidates, biomarker development, and animal care and use.

Skilled in resource limited management and conduct of all aspects of preclinical toxicology and biomarker development from discovery to product registration with emphasis on oncology and antiviral compounds. Partnered with outside companies to develop and implement biomarker strategies. Establishes acceptable daily exposure and occupational exposure levels for drugs and chemicals. Develops creative solutions and strategic guidance specific to company needs, resources and goals and improvements to ongoing processes in collaborative diverse team-based environments.

Education:

- BS, Life Sciences, Massachusetts Institute of Technology
- DVM, Veterinary Medicine, Iowa State University
- PhD, Experimental Pathology, Duke University

Work History:

Principal Toxicologist, Affygility Solutions, LLC – Broomfield, CO

- Establish occupational exposure levels and acceptable daily exposures limits to pharmaceutical and chemical manufacturers.

Principle Research Fellow (Vice-President Level),

Toxicology and Molecular Markers, OSI Pharmaceuticals – Boulder, CO

- Managed $8M toxicology and biomarker program budget supporting 8 toxicology studies, biomarker components of 10 clinical studies, and development of 2 companion diagnostics programs.
- Completed the analysis of biomarkers in RADIANT a world-wide 974 patient clinical trial in adjuvant NSCLC the largest single biomarker study to date in this indication. Presented the final biomarker data for RADIANT in an oral presentation to the World Congress on Lung Cancer, Amsterdam 2011.
- Served as biomarker representative on the SATURN (Tarceva for Maintenance in NSCLC) OSI fling team and the EURTAC (Tarceva in first-line NSCLC) regulatory team. Represented OSI at SATURN ODAC

meeting. Authored biomarker section of briefing document for the SATURN post approval commitment study which was presented and accepted by FDA.

- Chaired the OSI, Roche, Genentech Tripartite Biomarker Team. Drafted, presented, and gained approval from the Global Development Committee representing the 3 pharmaceutical companies of plans for the biomarker strategy and the development of companion diagnostics for Tarceva. Prioritized and coordinated the prioritization of biomarker testing in ongoing and planned Tarceva clinical trials. Completed investigative studies on the value and utility of EGFR IHC for detection of EGFR mutations. Contributed to the overall assessment of the utility of EGFR IHC, EGFR FISH, EGFR mutation and Kras mutations as predictive biomarkers for Tarceva in NSCLC (presented at WCLC 2011).
- Supervised a division of from 5 to 20 individuals spread between Boulder CO and Oxford England that initiated and completed over 100 internal or external GLP, investigative and discovery safety assessment studies including 5 INDs including oncology, diabetes / obesity, asthma, and macular degeneration compounds.
- Designed, conducted, and completed late-stage Tarceva toxicology studies, authored Preclinical NDA Section for Tarceva in 2nd line NSCLC and served as Lead Toxicologist for Tarceva at ODAC and FDA meetings that lead to successful approval in pancreatic cancer.
- Managed GLP and AAALAC Toxicology and Animal Care Division of over 20 people overseeing 2 successful FDA and AAALAC site inspections.
- Initiated OSI Biomarkers Program from concept to evaluation of over 20 biomarkers in more than 15 clinical trials covering 5 different compounds including development companion diagnostic tests, pharmacodynamics, predictive, prognostic, and response biomarkers.
- Designed, conducted, and published or presented research in over 20 papers / oral presentations / posters to the American Association of Cancer Research, American Association of Clinical Oncologists, Society of Toxicology, International Association of Study of Lung Cancer.

Director, Toxicology Safety Assessment and Animal Facility, Gilead Pharmaceuticals – Boulder, CO

- Managed a division responsible for the preclinical safety assessment of Gilead / Nexstar compounds, conducting mechanistic studies related to toxicities of candidate compounds and the appropriate care and use of animals.
- Designed, conducted, and completed of toxicology studies and authored preclinical the section of the NDA for Adefovir and Tenofovir NDA.
- Conducted and published 9 research studies on the mechanism of toxicity and action of nucleoside analog antiviral / anticancer agents.

Research Scientist, Eli Lilly and Company – Indianapolis, IN

- Responsible for conducting and publishing leading edge research into the mechanisms of compound induced carcinogenesis, mitochondrial toxicity, and anti-cancer efficacy, managing Lilly candidate

compounds through toxicology evaluations, and initiating processes of biomarker tissue collection and analysis.

- Initiated and completed conversion of the Nexstar / Gilead toxicology and animal facility to a GLP compliant and AAALAC approved program and facility evidenced by successful FDA site inspection and AAALAC accreditation.
- Designed, conducted, and published or presented over 30 studies to understand mechanisms of carcinogenesis of potential Lilly therapeutics, the mechanism of action of anti-cancer nucleoside analogs, the mechanism of toxicity of the anti-viral agent fialuridine (FIAU); the latter results used by the Institute of Medicine in evaluating the mechanism of lethal toxicity of FIAU in clinical trials. Toxicology project leader for antibody-toxin conjugate for the treatment of skin cancer in partnership with a biotechnology partner.

Training and Courses:

- Center for Creative Leadership Development
- Charles River Short Course
- Results Through People
- Society of Toxicology Continuing Education
- Midwest Toxicology Course
- Professional Affiliations
- American Association for Cancer Research
- Society of Toxicology
- Diplomat of American Board of Toxicology

Publications:

- RICHARDSON, F. C., DYROFF, M. C., BOUCHERON, J. A., AND SWENBERG, J. A. (1985). Differential repair of O4 -alkylthymidine following exposure to methylating and ethylating hepatocarcinogenesis. Carcinogenesis 6, 625-629.
- SWENBERG, J. A., RICHARDSON, F. C., BOUCHERON, J. A., AND DYROFF, M. C. (1985). Relationships between DNA adduct formation and carcinogenesis. Environ. Health Perspect. 62, 177-186.
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- DYROFF, M. C., RICHARDSON, F. C., POPP, J. A., BEDELL, M. A., AND SWENBERG, J. A. (1986). Correlation of O4-ethyldeoxythymidine accumulation, hepatic initiation, and hepatocellular carcinoma induction in rats continuously administered diethylnitrosamine. Carcinogenesis 7, 241-246.
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- RICHARDSON, F. C., BEAUCHAMP, R. O. JR., AND SWENBERG, J. A. (1987). Properties and biological consequences of alkylpyrimidine deoxyribonucleosides. Pharmacol. Therapeut. 34, 181-213.
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- SWENBERG, J. A., RICHARDSON, F. C., TYERYAR, L., DEAL, F., AND BOUCHERON, J. A. (1987). The molecular dosimetry of DNA adducts formed by continuous exposure of rats to alkylating hepatocarcinogens. Prog. Exp. Tumor Res. 31, 42-51.
- SWENBERG, J. A., RICHARDSON, F. C., BOUCHERON, J. A., DEAL, F. H., AND BELINSKY, S. A. (1987). High- to low-dose extrapolation: Critical determinants involved in the dose response of carcinogenic substances. Environ. Health Perspect. 76, 57-63.
- RICHARDSON, F. C., MORGAN, P. H., BOUCHERON, J. A., DEAL, F. H., AND SWENBERG, J. A. (1988). Hepatocyte initiation during continuous administration of diethylnitrosamine and 1,2-symdimethylhydrazine. Cancer Res. 48, 988-992.
- RICHARDSON, F. C., BOUCHERON, J. A., SKOPEK, T. R., AND SWENBERG, J. A. (1989). Formation of O6-methyldeoxyguanosine at specific sites in a synthetic deoxyribonucleotide designed to resemble a known mutagenic hotspot. J. Biol. Chem. 264, 838-841.
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- MING-SOUND TSAO, M.D., AKIRA SAKURADA, M.D., PH.D., JEAN-CLAUDE CUTZ, M.D., CHANG-QI ZHU, M.D., PH.D., SUZANNE KAMEL-REID, PH.D., JEREMY SQUIRE, PH.D., IAN LORIMER, PH.D., TONG ZHANG, M.D., NI LIU, M.SC., MANIJEH DANESHMAND, M.D., PAULA MARRANO, M.SC., GILDA DA CUNHA SANTOS, M.D., PH.D., ALAIN LAGARDE, PH.D., FRANK RICHARDSON, D.V.M., PH.D., LESLEY SEYMOUR, M.D., PH.D., MARLO WHITEHEAD, M.SC., KEYUE DING, PH.D., JOSEPH PATER, M.D., AND FRANCES A. SHEPHERD, M.D. (2005) Erlotinib in Lung Cancer — Molecular and Clinical Predictors of Outcome. New England Journal of Medicine. 353:133-144
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