



U.S. Environmental Protection Agency
Office of Research and Development
National Center for Computational Toxicology



***VACANCIES IN POST-DOCTORAL RESEARCH
ACCEPTING APPLICATIONS THROUGH October 9, 2009***

EPA's Office of Research and Development (ORD) is seeking post-doctoral candidates to join the National Center for Computational Toxicology (NCCT). The NCCT is located in Research Triangle Park, NC. The NCCT provides scientific leadership, understanding and tools related to the application of mathematical and computer models to technologies derived from computational chemistry, molecular biology and systems biology in order to improve the Agency's data reporting requirements, priority setting approaches to understanding chemical toxicity, and risk assessment approaches.

RESEARCH OPPORTUNITIES CURRENTLY AVAILABLE:

(SEE PROJECT DESCRIPTIONS AVAILABLE ON REVERSE SIDE)

- [NCCT-09-06 - Exposure Science for Chemical Prioritization and Toxicity Testing](#)
- [NCCT-09-07 - Chemical Structure Classifiers and Approaches for Toxicity Prediction in ToxCast™](#)
- [NCCT-09-08 - High Throughput Screening and Bioactivity Profiling of Nanomaterials](#)
- [NCCT-09-09 - Understanding the Sources and Impact of Uncertainty in Predictive Models of Toxicity from the ToxCast™ Program](#)

UNSURPASSED FEDERAL EMPLOYEE BENEFITS:

- Salary range-- **\$58,144 to \$90,610 depending on experience**
- Full **three-year** appointments, with option to extend to **four years**
- Paid relocation to EPA duty location
- Vacation and sick leave
- Federal health benefits, life insurance, and retirement program
- Travel to professional scientific meetings
- Active Post-doctoral Trainee Organization at RTP, NC

EASY APPLICATION PROCESS: PREFERENCE IS GIVEN TO U.S. CITIZENS

- Up-to-date Curriculum Vitae
- Letter of recommendation from your research advisor or comparable official
- Cover letter indicating positions and locations of interest
- DD-214, if claiming veteran's preference

E-mail the material listed above to: ordpostdocapps@epa.gov

To learn more about our current research projects and application requirements, please visit the NCCT website at: <http://www.epa.gov/comptox/> or contact Ms. Dorothy Carr at (800) 433-9633, or via email at carr.dorothy@epa.gov.

*The U.S. EPA is an Equal Opportunity Employer
and Provides Reasonable Accommodations to Applicants with Disabilities*

NCCT-09-06 Exposure Science for Chemical Prioritization and Toxicity Testing The post-doctoral associate selected for this research project will participate in developing novel tools for characterizing and predicting potential for biologically-relevant human exposure to chemicals. The EPA's National Center for Computational Toxicology has identified the need to include exposure information for chemical prioritization, modeling system response to chemical exposures across multiple levels of biological organization, and linking information on potential toxicity of environmental contaminants to real-world health outcomes. A critical need is the development of robust analytical approaches that use a wide range of human exposure data, product use information, and modeled human behavior to systematically prioritize potential for exposure based on chemical properties, product lifecycle, individual and population characteristics. Tools are required to characterize and classify thousands of chemicals in a rapid and efficient manner. This work will build on related international efforts to classify and prioritize chemicals for risk assessment (e.g., Canadian DSL, REACH, ChAMPS, etc). *Scientific Contact: Elaine Cohen Hubal Email: hubal.elaine@epa.gov*

NCCT-09-07 Chemical Structure Classifiers and Approaches for Toxicity Prediction in ToxCast™ This post doctoral associate will apply cheminformatics concepts to develop novel methods for chemical classification and toxicity prediction in association with the ToxCast™ and Tox21 research projects. ToxCast™ is generating high-throughput screening (HTS) data for 1,000 chemicals in over 500 biochemical, cell-based, and model organism assays. Tox21 is a collaboration between EPA, NTP (National Toxicology Program), and NCGC (NIH Chemical Genomics Center) that is generating HTS data for a larger set of upwards of 10,000 compounds of environmental interest in an expansion of the ToxCast™ paradigm. Initial modeling efforts have focused on developing predictive toxicity signatures relating HTS results to reference *in vivo* toxicity endpoints. A key requirement to the success of such efforts will be the integration of chemical clustering concepts based on chemical properties, reactivity and metabolism, with biologically-informed clustering derived from toxicity, mechanistic and HTS data. A key difference in this approach from traditional structure-activity relationship (SAR) approaches is the explicit incorporation of HTS biological data in guiding selection of chemical classes, and refinement of traditional chemistry-based classes based on biological data. We envision a layered approach whereby chemical classifications are flexible and tailored to the compound and biological activity space under consideration. This research will take advantage of data mining approaches and informatics methods being developed within and outside the NCCT. The associate will develop and apply these methods to both the ToxCast™ and larger Tox21 chemical sets in an effort to refine toxicity predictions for chemicals and chemical classes and support chemical prioritization for more extensive toxicity testing. *Scientific Contact: Ann Richard Email: richard.ann@epa.gov*

NCCT-09-08 High Throughput Screening and Bioactivity Profiling of Nanomaterials The post-doctoral associate selected for this research project will participate in developing novel tools for characterizing the bioactivity for a variety of classes of nanomaterials. The EPA's National Center for Computational Toxicology (NCCT) has identified the need to include nanomaterials in its ToxCast™ chemical prioritization program, evaluating the applicability of ToxCast™ assays and predictive toxicity models. This approach will utilize extensive *in vitro* characterization of biological activity of tested materials and apply computational models to characterize biological pathway activity. A critical need is establishing appropriate material handling methods for testing nanomaterials in the ToxCast™ *in vitro* screening assays. In addition, the coordination of physico-chemical characterization of nanomaterials with key partners is required to provide appropriate understanding of the materials being tested and provide data for structure-activity relationships. This work will be coordinated with related national and international efforts to classify and prioritize nanomaterials for hazard (e.g. OECD, EU FP7 nanomaterials risk assessment). ToxCast™ high throughput screening (HTS) data, physico-chemical properties, and all other accessible *in vitro* and *in vivo* toxicity data will be entered into NCCT databases and used to develop statistical and biological models. *Scientific Contact: Keith Houck Email: houck.keith@epa.gov*

NCCT-09-09 Understanding the Sources and Impact of Uncertainty in Predictive Models of Toxicity from the ToxCast™ Program The goal of the EPA ToxCast™ program is the prediction and understanding of environmental chemical toxicity. At the core is an effort to build predictors of a chemical's propensity to produce various kinds of toxicity. Predictors so far have been statistical models such as would be derived from machine learning methods (regression, neural networks, support vector machines, etc.) but may well be informed by more biological considerations in the future. The inputs to the predictors are parameters such as IC50s derived from a wide range of *in vitro*, high-throughput screening (HTS) biological assays. The predictors themselves are trained on data for a set of environmental chemicals with animal toxicity studies. Summaries of the results of the *in vivo* animal toxicity studies are used as the targets for training the predictors. A major issue with this approach is a lack of understanding of the variability inherent in the experimental results, *in vitro* and *in vivo*, and how that affects the usefulness of the resulting models. Ultimately, ToxCast™ results will be used for prioritizing chemicals for further testing, and potentially for more quantitative risk assessment purposes. It is critical for such applications that the uncertainties of ToxCast™ outputs be quantified. While the naive output of a predictor may be a ranking of chemicals in terms of their predicted propensity to cause a given toxicity, when uncertainty is properly taken into account, that ranking may turn into a partial ranking, or a set of rankings and associated weights (e.g., the most likely ranking of chemicals A – D may be 1,2,3,4; while an almost equally supported ranking is 1,3,2,4; in this example, the data do not really distinguish the order of B and C relative to this sort of toxicity). Uncertainty arises in ToxCast™ from three components: through the HTS assays, both through biological variability and the measurement process; through uncertainty about the quantitative characterization of whole-animal toxicity, and uncertainty about the predictors themselves, which are derived from a kind of fitting process. The goal of this project is to quantify and understand all three sources of uncertainty, using a combination of conventional statistical methods, and mechanistic models to characterize biological variability, variability introduced by the measurement processes, and uncertainty about the choice of prediction model. *Scientific Contacts: Woodrow Setzer and Richard Judson Emails: setzer.woodrow@epa.gov and judson.richard@epa.gov*