Code Number and Title:

LRI-C3: Epigenetics: Normality in Toxicologically Relevant Species

Background

Epigenetic evaluation is a complex and expanding area of research with the potential to help understand the mode of action by which substances produce toxicological effects. As with any new technology, and epigenetics is no exception, there is an inherent insecurity concerning the reproducibility of results when different laboratories are carrying out measurements. In addition, as there are few historical data available currently there are knowledge gaps about natural fluctuations and the sensitivity of results that might occur during an experiment. Moreover, recent advances in knowledge and technology indicate that earlier epigenetics results may have suffered from inadequate measurement in as much as that DNA-methylation may have been incorrectly assigned. Methylated DNA appears to be subject to further transformation through oxidative processes leading to an elimination of the repressive function of the methylated site.

Objectives

The objective of this project is to produce reference methylomes for several rodent strains commonly used in toxicology using sequencing methodologies.

Scope

After consolation with the literature and the Roadmap epigenomics projects the researchers will provide a proposal focused on DNA methylation mapping for a series of normal laboratory mouse and rat strains. A minimum of two strains each of mice and rats commonly used in toxicological investigations are preferred. Selection of the age, sex and diet of the animals and other confounding factors will be left to the discretion of the researchers but applicants must justify their decisions. Researcher need to keep in mind that the overall goal of the project is to assess “normality” for epigenetics. Similarly the choice of the organ(s) for analysis will be left to the applicant but again the researchers should justify the choice of organ(s) and address the issue of cell heterogeneity within the organs chosen, and how this will this affect the analysis. The protocols for analysis should be based on the standard published methodology with focus on whole genome rather than specific regions. Justification of the technique used by the researchers should be included with the application.

Researchers are encouraged to present the results of their work at scientific symposia and publish in peer reviewed scientific journals and submit their data to appropriate on-line repositories. An outline of delivery of the science should be included in the proposal. Progress of the research will be reviewed periodically at agreed times with CEFIC LRI.

Deliverables

The final report will comprise an executive summary (2 pages max), a main part (max. 50 pages) and a detailed bibliography. It is expected that the findings will be developed into a peer reviewed publication, following presentation at a suitable scientific conference.

Fit with LRI objectives/Possible regulatory and policy impact involvements/ Dissemination

Applicants should provide information on the fit of their proposal with LRI objectives and an indication on how and where they could play a role in the regulatory and policy areas. Dissemination plans should also be laid down.

Cost and Timing

Start in May 2014, duration 1-2 years

Budget in the order of €350.000

Partnering/Co-funding

Applicants should provide an indication of additional partners and funding opportunities that can be appropriately leveraged as part of their proposal. Partners can include, but are not limited to industry, government/regulatory organizations, research institutes, etc. Statements from potential partners should be included in the proposal package.

DEADLINE FOR SUBMISSIONS: 10 January 2014

Please see www.cefic-lri.org for general LRI objectives information, project proposal form and further guidance for grant applications. For further assistance do not hesitate to contact lri@cefic.be.