

















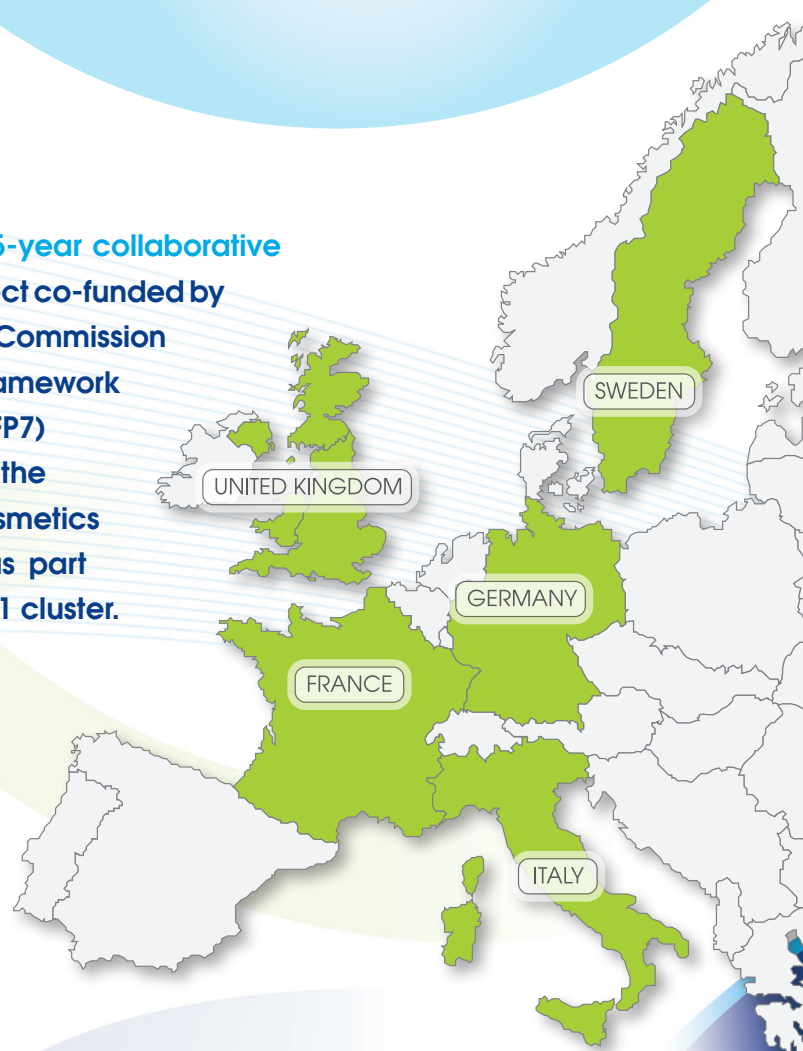
PARTNERS

The consortium brings together thirteen internationally renowned research teams from France, Germany, Italy, Sweden and United Kingdom, including academic research laboratories, one large pharmaceutical industry, three small and medium enterprises (SMEs) and two contract research organisations (CROs).

Representatives of Sanofi-Aventis, Bayer Schering Pharma, F. Hoffman-La Roche, GlaxoSmithKline and L'Oréal/COLIPA are members of the SCR&Tox independent "Industrial and Regulatory Consultative Body", providing a direct link to the project's main stakeholders. In addition, an ethics specialist accompanies our research activities using human pluripotent stem cells.

COUNTRY	PARTNER INSTITUTION	SCIENTIST
Research		
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SCR&Tox is a 5-year collaborative research project co-funded by the European Commission within its 7th Framework Programme (FP7) and COLIPA, the European Cosmetics Association, as part of the SEURAT-1 cluster.



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For more information please visit our website
www.scrtox.eu



STEM CELLS for relevant efficient extended and normalized TOXICOLOGY

Using derivatives of human pluripotent stem cell lines, SCR&Tox seeks to provide *in vitro* cell-based test systems for predicting toxicity of drugs, chemical compounds and cosmetic ingredients.



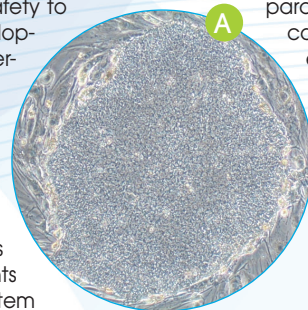
SCR&Tox is co-funded by the European Commission within its FP7 Programme and COLIPA, the European Cosmetics Association, as part of the SEURAT-1 cluster. Grant Agreement number HEALTH-F5-2010-266753.

CONTEXT

In the development of products for use by humans, it is vital to identify compounds with toxic properties at an early stage of their development, in order to avoid spending time and resources on unsuitable and potentially unsafe candidate products. New cosmetic products launched on the European market need to be assessed for safety to human health. The development of non-animal alternative methods represents a considerable scientific challenge.

SCR&Tox aims at addressing the unmet need for testing methods to predict toxicity of drugs, chemicals and cosmetic ingredients and human pluripotent stem cell lines offer a unique opportunity to develop a wide variety of human cell-based test systems as they may be expanded indefinitely and triggered to differentiate into any cell type. SCR&Tox has been designed to make use of these two attributes to provide *in vitro* assays for predicting toxicity of pharmaceutical compounds and cosmetic ingredients and to address all issues related to biological and technological resources to meet this goal.

SCR&Tox is integral part of the European research initiative SEURAT-1 (Safety Evaluation Ultimately Replacing Animal Testing) co-funded by EU-FP7 HEALTH programme and the European Cosmetics Association (COLIPA). The SEURAT-1 cluster includes six research projects aiming at a common strategy "towards the replacement of current repeated dose systemic toxicity testing in human safety assessment".



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OBJECTIVES

SCR&Tox aims at providing proof of concept on the use of pluripotent stem cell lines for identifying "toxicity pathways", i.e. key signaling pathways, the perturbations of which result in adverse health effects, and for setting-up assays for assessing risks to trigger those pathways. This will be carried out in parallel in five main target organs for drug and cosmetic toxicity, namely the liver, heart, epidermis, nervous and musculoskeletal system.

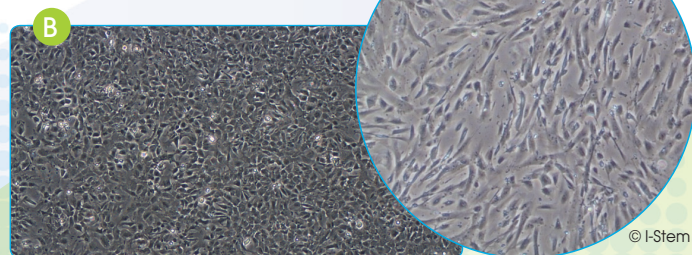
SCR&Tox main objectives are to:

1. optimise pluripotent stem cells biotechnology for large-scale multi-systemic assays,
2. develop appropriate techniques to engineer genetically pluripotent stem cell lines,
3. develop de-differentiation and reprogramming as a tool to explore human polymorphism *in vitro*,
4. develop technologies to identify molecular partners of toxicity pathways,
5. engineer specific "tool"-cell lines dedicated to screening of specific toxicity pathways,
6. explore all parameters of the toxicant administration (dose, duration, repetition, etc.) that may participate to adverse health effects,
7. in order to finally demonstrate the feasibility of the developed toxicity assays within an industrial framework.

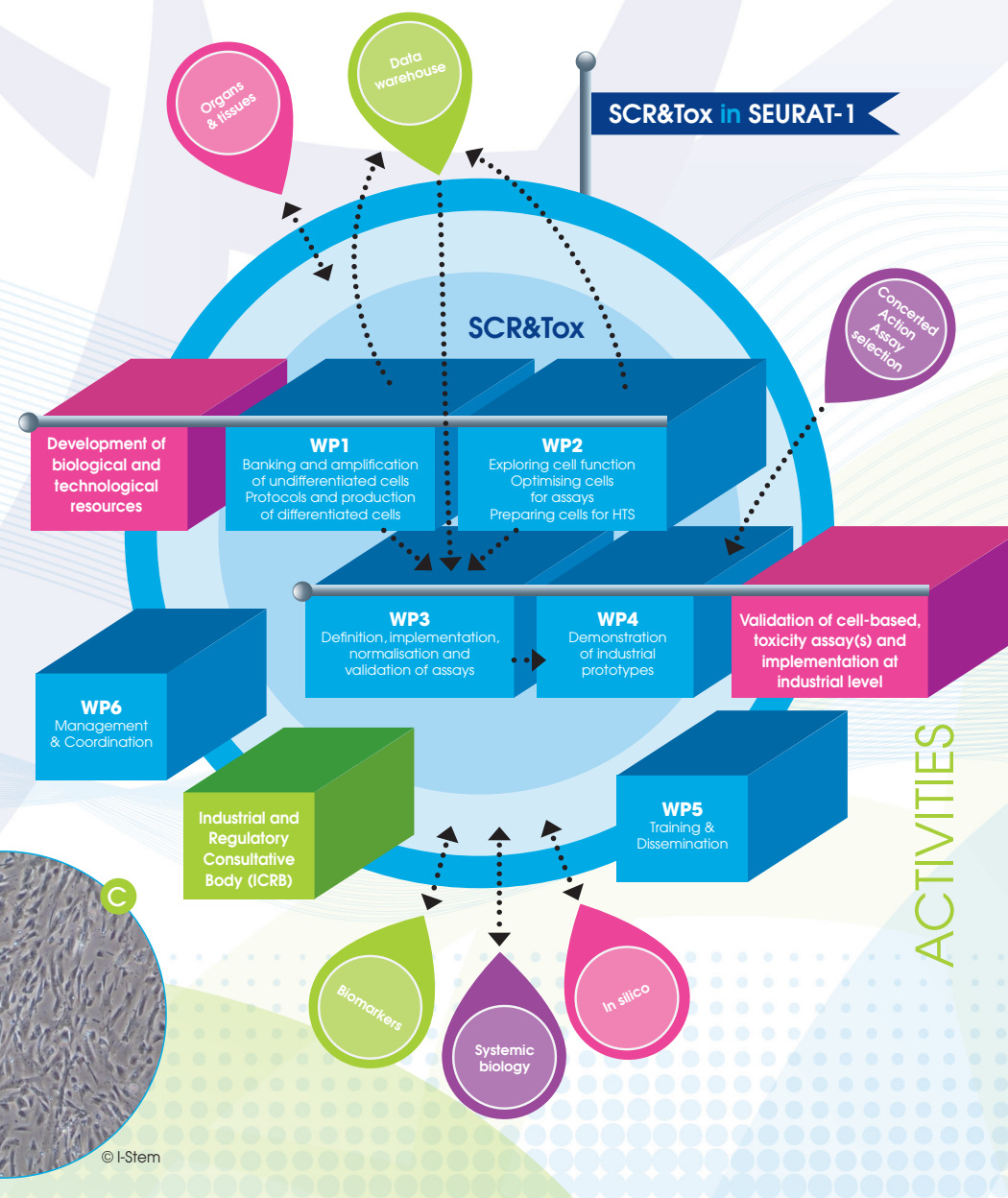
STRATEGY

The SCR&Tox programme has been structured to provide all necessary resources and technologies for exploring derivatives of pluripotent stem cell lines as relevant and reliable model systems that can be robust and scalable in order to meet the challenges of industrial-scale screens. Human pluripotent stem cells will be obtained and expanded from a diversity of donors, to obtain a glimpse of the effects of the genetic diversity. They will be differentiated into five different cell types representing organs of particular interest for toxicology (liver, heart, brain, skin and muscle). Methodologies will be developed for exploring molecular mechanisms perturbed by toxicants. At half-term of the project, these resources should be ready and proof of concepts will then be sought by developing toxicity assays using them, first on the bench then, at a final stage, on industrial platforms.

SCR&Tox will be tightly associated to the other consortia of the SEURAT-1 research cluster, sharing biological, technological and methodological resources. Proof of concept of the proposed pluripotent stem cell-based assays for toxicology will be provided on the basis of toxicity pathways and test compounds identified by other consortia.



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EXPECTED OUTCOMES

- SCR&Tox will lead to novel tools for *in vitro* testing to replace or reduce animal experimentations in predictive toxicology for pharmaceutical compounds and cosmetic ingredients.
- SCR&Tox will bring proof of concept of predictive toxicology testing at industrial scale on the basis of cell-based assays using human pluripotent stem cell derivatives.
- SCR&Tox research will lead to tangible advances in scientific approaches: i) pluripotent stem cells provision and differentiation into derivatives along different lineages of interest, ii) genetic engineering as a way to provide cells with additional properties in view of an industrial use and iii) gene and protein profiling as well as exploration of dynamic functions.
- In parallel, SCR&Tox will contribute to specific training experiences for the next generation of toxicologists, through technology transfer to stakeholders in the pharmaceutical and cosmetic industry, in particular through hands-on training at partners' sites and assistance for setting-up laboratories in stakeholders' plants and for regulatory agencies to adapt to the new paradigm.

Photographs legends

Human pluripotent stem cells: A colony of human embryonic stem cells (A) can be differentiated into many lineages including neural stem cells (B), mesodermal progenitor cells (C) and basal keratinocytes.