

Safety Evaluation Ultimately Replacing Animal Testing



What is SEURAT-1?

*Michael Schwarz, Eberhard Karls University of Tübingen, Germany,
on behalf of COACH and the SEURAT-1 Consortium*



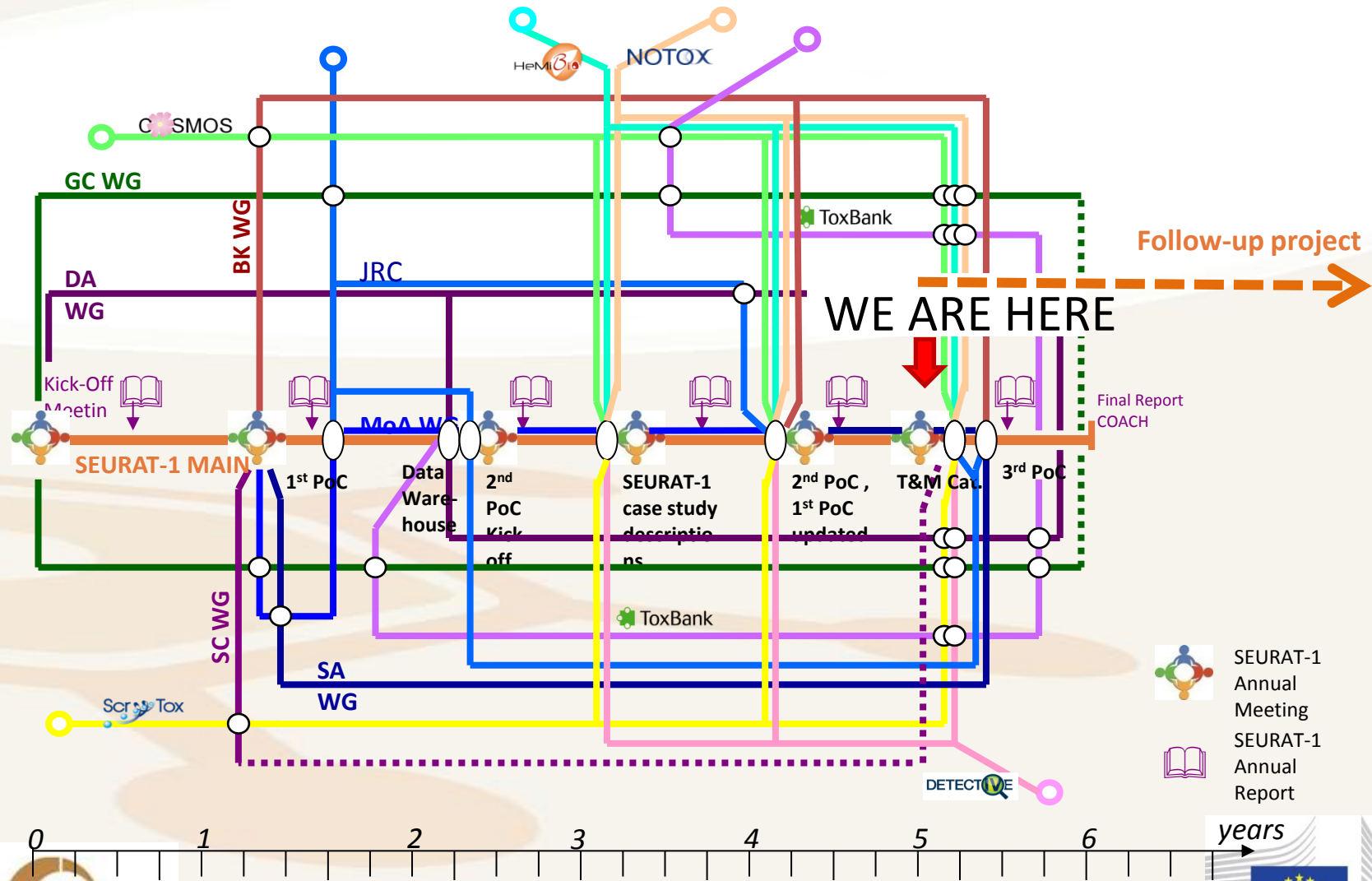
Towards replacement of *in vivo* repeated dose systemic toxicity testing



- Cluster of seven collaborative projects, including a coordination action
- 50 million Euro investment
- Co-financed by the European Commission and Cosmetics Europe (unique PPP)
- 5 (6) year programme (start: Jan. 2011)



<http://www.seurat-1.eu/>

The SEURAT-1 roadmap



-  SEURAT-1 Annual Meeting
-  SEURAT-1 Annual Report

70 partners

in silico toxicology

PHARMATROPE Douglas Connect  **Karolinska Institutet**

 **ToxBank**  **IOFA consult**

 **NIBSC**  **MARIO NEGRI**
ISTITUTO DI RICERCHE FARMACOLOGICHE

 **Leadscope**

 **Imperial College London**  **Vrije Universiteit Brussel**

 **MEDIZINISCHE UNIVERSITÄT INNSBRUCK**  **DETECTIVE**
Detection of Endpoints and Biomarkers for Repeated Dose Toxicity Using In Vitro Systems

 **Fraunhofer ITEM**  **Universiteit Leiden**

 **ProteoSys**  **DFK**  **Deutsches Forschungszentrum für Künstliche Intelligenz GmbH**

 **QureTEC**  **Maastricht University** *Leading in Learning!*  **iSCS**  **Roche**



 **Altamira**  **SIN**
soluzioni informatiche

 **JMU**  **Henkel**

 **Open for Innovation**  **KNIME**

 **UNIVERSITY OF BRADFORD**
MAKING KNOWLEDGE WORK

 **ILSI Europe**  **COSMOS**

 **JRC EUROPEAN COMMISSION**  **INERIS**  **MERCK**

 **insilico biotechnology**  **IU**  **Molecular Networks**
Inspiring Chemical Discovery

 **UNIVERSITÄTSKLINIKUM REGensburg**  **Fraunhofer**  **Vrije Universiteit Brussel**

 **UNIVERSITY OF OSLO**  **HemiBio**  **imec**

 **UNIVERSITY OF TROMSØ**  **KATHOLIEKE UNIVERSITEIT LEUVEN**  **medicyte**

 **IDIBAPS**  **MHH**
Medizinische Hochschule Hannover

 **collectis**  **AstraZeneca**

 **Karolinska Institutet**  **ScribTox**  **universität bonn**

 **AVANTEA**  **European Commission**  **CiToxLAB**

 **UNIVERSITÄT LEIPZIG**  **COVANCE SOLUTIONS MADE REAL**

 **InsermTransfert**

 **ARTTIC**
INTERNATIONAL ASSOCIATION OF TOXICITY RESEARCHERS

 **COACH**

 **EBERHARD KARLS UNIVERSITÄT TUBINGEN**  **JRC EUROPEAN COMMISSION**

 **cnrs**  **EUSERVICE**  **NETHERLANDS CANCER INSTITUTE**
ANTON VAN LEEUWENHOOEK

 **BIOPREDIC INTERNATIONAL**  **UNIVERSITÄT DES SAARLANDES**

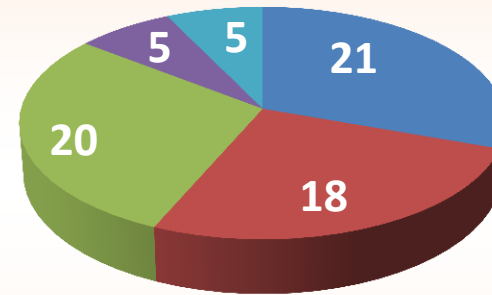
 **insilico biotechnology**  **NOTOX**  **Cambridge Cell Networks**

 **מכון ויצמן למדע**
WEIZMANN INSTITUTE OF SCIENCE  **NKI-AVL**  **Deutsches Forschungszentrum für Künstliche Intelligenz GmbH**

 **Karolinska Institutet**  **IDDo**



Where do partners come from?



- SME
- University
- Research Institution
- Industry

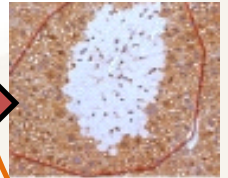
Conventional method for repeated dose systemic toxicity testing



We need better science!



alive
healthy



?



Test compound: 28 / 90 days



dead
diseased



.....

SEURAT-1 - The Strategy



*The SEURAT strategy is to adopt a toxicological **mode-of-action framework** to describe how any substance may adversely affect human health, and to use this knowledge to develop complementary theoretical, computational and experimental (in vitro) models that predict quantitative points of departure needed for safety assessment.*

Mode of action-defined test compounds



Hypothesis-driven development of assay systems



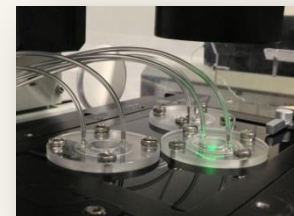
Long-term aim:
Innovative safety assessment based on understanding of adversity at the molecular / cellular level

SEURAT-1 - the new approach



Integrative approach:

- *in vitro* experimental data from human cells exposed to chemicals using sophisticated experimental systems (e.g. organ-on-a-chip)
- Computer methods to predict pharmacokinetic behaviour, target interaction, etc.....



The Hebrew University of Jerusalem



Mark
Cronin



Catherine
Verfaillie



Marc
Peschanski



Jürgen
Hescheler



CSMOS

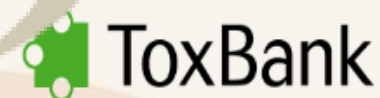


NOTOX

COACH



SEURAT-1



Elmar
Heinzle



Bruno
Cucinelli



Barry
Hardy



The building blocks of SEURAT-1



The **stem cell project**

Development of stem cell differentiation protocols for providing human-based organ specific target cells



The ***in vitro* liver project**

Development of a functional liver co-culture system using hepatic microfluidic bioreactors



The **biomarker project**

Detection of endpoints and biomarkers for repeated dose toxicity using *in vitro* systems



The ***in silico* toxicology project**

Delivery of computational tools to predict effects of chemicals based on *in silico* calculations and estimation techniques



The **systems biology project**

Development of systems biological tools for organotypic human cell cultures



The **data management project**

Supporting integrated data analysis and servicing of alternative testing methods in toxicology

COACH

The **Coordination Action**

Cluster level Coordinating and Support Action



SEURAT-1 cross-project Working Groups



- Gold Compound W.G.
- Data Analysis W.G.
- Mode-of Action W.G.
- Biokinetics W.G.
- Stem Cell W.G.
- Safety Assessment W.G.

Arch Toxicol (2014) 88:2099–2133
DOI 10.1007/s00204-014-1410-8

REVIEW ARTICLE

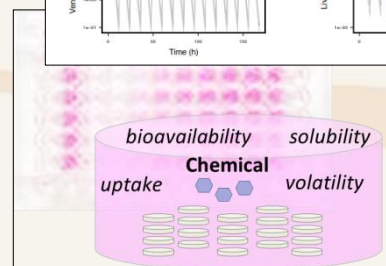
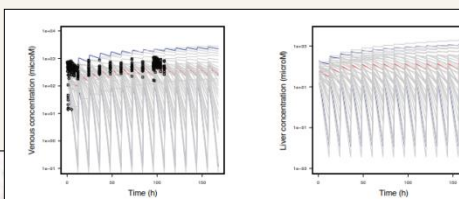
SEURAT-1 liver gold reference compounds: a mechanism-based review

Paul Jennings · Michael Schwarz · Brigitte Landesmann · Silvia Maggioni · Marina Goumenou · David Bower · Martin O. Leonard · Jeffrey S. Wiseman

TOXICOLOGICAL SCIENCES 136(1), 97–106 2013
doi:10.1093/toxsci/kft177
Advance Access publication August 14, 2013

Development of an Adverse Outcome Pathway From Drug-Mediated Bile Salt Export Pump Inhibition to Cholestatic Liver Injury

Mathieu Vinken,^{a,1} Brigitte Landesmann,[†] Marina Goumenou,[‡] Stefanie Vinken,[‡] Imran Shah,[§] Hartmut Jaeschke,[¶] Catherine Willett,^{||} Maurice Whelan,[†] and Vera Rogiers^{*}



Adverse Outcome Pathway Wiki

Page | Discussion

Aop:38
Main Page > AOP List > Aop:38


AOP Title
Protein Alkylation leading to Liver Fibrosis
Short name: Protein Alkylation to Liver Fibrosis

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Status
Under development: Do not distribute or cite.
OECD Project 1.14: The Adverse Outcome Pathways from protein alkylation to liver fibrosis.
This AOP page was last modified on 6/19/2015.
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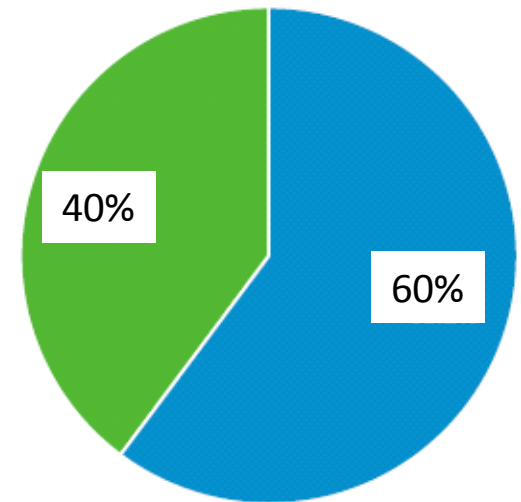
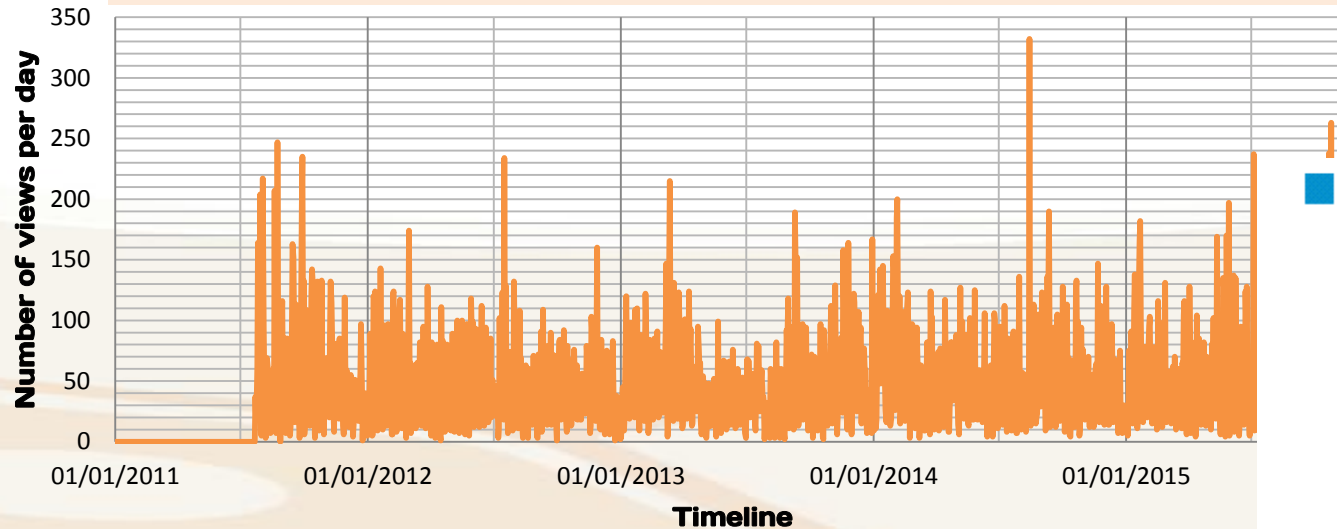
Actions
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Tools

 **ToxBank**
**General Quality and Regulatory Criteria for
Establishment and Dissemination of human
Pluripotent Stem Cell Lines (hPSCs)**

SEURAT-1 visibility: Website visits



Website views / day (2011 – 2015)



SEURAT-1: Doctoral theses (2011-2015)



graduated students:
44



(2011-2015):

➤ patents: **5**

➤ publications: **336**

Impact Factor > 10	
<i>Journal</i>	<i>Number</i>
Nature	1
Nature Chem. Biol.	1
Nature Biotechn.	1
Nature Methods	1
Gastroenterology	1
J. Hepatology	5
Hepatology	3
Gut	2

What is SEURAT-1?



A Success Story!



Thank you!

