OpenRiskNet

RISK ASSESSMENT E-INFRASTRUCTURE

WP4 Service Integration

Danyel Jennen (UM)

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OpenRiskNet: Open e-Infrastructure to Support Data Sharing, Knowledge Integration and *in silico* Analysis and Modelling in Risk Assessment

Project Number 731075



WP4 Objectives

- Integration of a representative number of services as best-practice examples with the corresponding step-by-step documentation
- Harmonisation of approaches to provide information on service status, capabilities and requirements over the interoperability layer
- Adoption of the data schemata and deployment as well as authentication & authorisation (optional) options proposed by WP 3 and 2, respectively
- Guarantee the error-free communication and integration of the services in the infrastructure and provide maintenance of the service throughout the duration of the project

WP4 Service Integration

ID	Title	Partners involved	Start month	End Month	Deliverables
T4.1	Toxicology, Chemical Properties and Bioassay Databases	UM, UoB, DC, NTUA	7	24	D4.1; D4.2; D4.3; D4.4
T4.2	Omics Databases	UM, UoB, CRG, DC, NTUA, CRG	7	24	D4.1; D4.2; D4.3; D4.4
T4.3	Knowledge Bases and Data Mining	UM, UoB, DC, NTUA, Fraunhofer	7	24	D4.1; D4.3; D4.4
T4.4	Ontology Services	UoB, UM	7	24	D4.1; D4.3; D4.4
T4.5	Processing and Analysis	DC, CRG, NTUA, UM, UoB, IM	7	24	D4.1; D4.3; D4.4
T4.6	Predictive Toxicology	JGU, NTUA, INERIS, UoB, UM, UU, IM	13	30	D4.3; D4.4
T4.7	Workflows, Visualisation and Reporting	IM, UU, UoB, DC, JGU	13	30	D4.3; D4.4



WP4 Deliverables

ID	Title	Due month	Lead partner	Туре	Dissemination level
D4.1	Report of the Service Integration with OpenRiskNet (Initial Deployment)	12	υм	Report	Public
D4.2	Report of the Service Integration with OpenRiskNet (Intermediate Report)	24	UoB	Report	Public
D4.3	Report of the Service Integration with OpenRiskNet (Final Report)	36	им	Report	Public
D4.4	Report on Re-Identification Risks and Private by Design Risk Management	12	DC	Report	Public



WP4 Milestones

ID	Title	Due month	Lead partner	Means of verification
N/I C /	Adoption of the data schemata and deployment options by prototype services	18	UM	Well documented reference implementation of services



WP4 Performance Metrics

Title

T4.1: Successful integration of >= 6 (until M18) and >= 10 (until M36) services

T4.2: Successful integration of >= 2 (until M18) and >= 4 (until M36) services

T4.3: Successful integration of >= **4** (until M18) and >= **10** (until M36) services

T4.4: Successful integration of >= 1 (until M18) and >= 2 (until M36) services

T4.5: Successful integration of >= 4 (until M18) and >= 6 (until M36) services

T4.6: Successful integration of >= **6** (until M18) and >= **10** (until M36) services

T4.7: Successful integration of >= 2 (until M18) and >= 3 (until M36) services



Services from ORN proposal a.k.a. Table 1.1

Service		Partner		Third			Service			Partner		Third			,						
Toxicolog		rvice	_		Pa	rtner		Third		Service	е	I s		Partner		Third			t		
eChemPo	*01	mics D		Service	-		P	artner		Third	2		Service		F	artner	Third Party				
ChEMBL	dix	(a		Knowled	dç	Service			Pa	rtner		Third Party	Service		е		Partner		Third Party		_
ChEBI	EG	6A		AOP KB		Ontolo	gy	Service			P	artner	rtner Thi		(2000)	Service	ı		Partner	Third	
ChemSpid		ne exp	OI	CTD		Ontolog	y	Proces		Service							Third Service		ce P		Partner
PubChem.	oChem Triple An		nn			Process	essii		1				Partv						Partv		
DrugBank		0	U	Tool	~·+			Toxygat	tes	Workflo	w.	Service	Partner		tner	Third Service Party			Partner		
ToxNet			U	WikiPath	ıwa	ays	U	Omics of	1000	Squonk		Predicti	ve	Toxicolo	gy			7			
				Pathway Annotation Tool		U			Bioclipse Laz		Nano Lazar II		IST		BBRC		BBRC		JGU		
				3.50	1 1001		Network	k m aly: Risk21 Ap		۸n			r I	IST		-\$1 20		LAST-PN	1	JGU	
				Mapping		U	(DIME/C	Coc	KISKZ I /	Αþ	PubChe	om Dood		d IST		10		FCDE		JGU	
			Tool		10000 2700		Image A				Across	111 7	rcau I	IO I				TODE		300	
OpenRis	skN	let		Chemist	ry	7	U	GO des		tor	N	PBPK m	od	el l	INE	RIS			PSCG		JGU

WP4 Performance Metrics (GA December 2018)

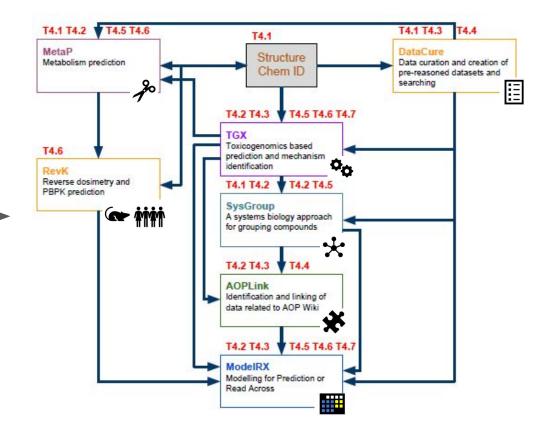
Title	Status M24	In progress*
T4.1: Successful integration of >= 6 (until M18) and >= 10 (until M36) services	5	10
T4.2: Successful integration of >= 2 (until M18) and >= 4 (until M36) services	1	5
T4.3: Successful integration of >= 4 (until M18) and >= 10 (until M36) services	4	4
T4.4: Successful integration of >= 1 (until M18) and >= 2 (until M36) services	-	3
T4.5: Successful integration of >= 4 (until M18) and >= 6 (until M36) services	2	3
T4.6: Successful integration of >= 6 (until M18) and >= 10 (until M36) services	6	6
T4.7: Successful integration of >= 2 (until M18) and >= 3 (until M36) services	3	3

^{*}New services from implementation challenge not yet included



Tasks ↔ Case Studies

ID	Title
T4.1	Toxicology, Chemical Properties and Bioassay Databases
T4.2	Omics Databases
T4.3	Knowledge Bases and Data Mining
T4.4	Ontology Services
T4.5	Processing and Analysis
T4.6	Predictive Toxicology
T4.7	Workflows, Visualisation and Reporting





Service integration procedure → 8 operations

- 1. Utilising the OpenRiskNet APIs to ensure that each service is accessible to our proposed interoperability layer;
- Annotating the services according to the semantic interoperability layer concept using defined ontologies;
- 3. Containerising the services for easy deployment in virtual environments of OpenRiskNet instances;
- 4. Documenting the scientific and technical background;
- 5. Deploying the service into the OpenRiskNet reference environment;
- 6. Listing the service in the OpenRiskNet discovery services;
- 7. Listing in other central repositories like eInfraCentral, bio.tools and TeSS (ELIXIR);
- 8. Providing legal and ethical statements on how the service can be used.



Task	Services integrated*	1	2	3	4	5	6	7	
	Squonk services for chemical property prediction	/		х		х			
	cpLogD		/	х	х	/			
	Modelling Web			х		х			Γ
	CDK-Depict			х					
	Chemidconvert	х		х	х	х	x		
4.1	eNanoMapper - nanomaterial database	х							Γ
4.1	FDA Estrogenic Activity Database	х	/	х	х	х	х		Γ
	MetPred	х		x	х	х	х		Γ
	LTKB			х		х			Γ
	ToxRefDB	х		х					Γ
	ToxCast/Tox21 summary data	х		х	х				Γ
	Tox21 sample specific data	х							Γ
	TG-GATEs	х		х					
	Toxygates	х		х					Γ
	diXa (via BioStudies)	/							Γ
4.2	Gene Expression Omnibus (GEO)	/							Γ
	ArrayExpress	/							Γ
	EGA Beacon							х	Γ
Ī	EGA Metadata API				х			х	Г

*New services from implementation challenge not yet included

Task	Services integrated*	1	2	3	4	5	6	7	8
	BridgeDb	х		х		х		х	
	Data mining algorithms through Jaqpot	х	/	х	Х	х	х	х	/
	Data mining algorithms through JGU Weka	х	х	х	х	х	х	х	,
4.3	SCAIView Scientific Literature Database	/	/	х	/				
1.0	WikiPathways	/		/	х	/			
	AOP-Wiki	/		/		/			
	eNanoMapper - nanomaterial database	х		х	х	х	х	х	
	Jenkins: ontology building and testing								
4.4	Ontology Lookup Service (OLS)	/	/	х	/				Г
	Ontology Annotation Services (BELIEF Text Mining)	/	/	х	/				
	Jaqpot processing and analysis services	х	/	x	x	x	х	х	Г
4.5	CDK descriptor calculation service	х	/	х	x	х	х	х	Г
4.5	PROAST and TCPL dose response modelling service	х							
	P450 SOM predictor	х	х	х	х		х		
	WEKA REST Service	х	х	х	х	x	х	х	
	Lazar Toxicity Predictions	х	/	х	Х	х	х		
4.6	Jaqpot predictive modelling services	х	/	X	X	X	х	х	
4.0	Jaqpot applicability domain services	х	/	Х	Х	х	х	х	
	Jaqpot PBPK modelling services	х	/	X	Х	х	х	х	
	httk package for PBPK modelling service	х	/	/	/	/	/		
	Squonk Computational Notebook	/		х		x			L
4.7	Jupyter notebooks			х		х			Ĺ
	Nextflow			х		x			



x = full compliance, / = partly implemented

OpenRiskNet Services

LOGIN INSTRUCTIONS →

THE REFERENCE ENVIRONMENT →

SETTING UP YOUR OWN VRE ->

OpenRiskNet services

Submit a service

Category

•

Service type



User type



Targeted users



Filter

Reset

OCHEM models

Prediction of chemicals

Prediction of different endpoints

Provided by: BigChem GmbH

Type: Trained model

Applicability domain: Predictive toxicology

Topic: Chemical properties, Risk assessment, Structure-activity

relationship (SAR / QSAR), Predictive modelling Biological area: NOAEL/LOAEL, Acute toxicity

AOP-DB SPARQL Endpoint

This service is a Virtuoso SPARQL endpoint that is loaded with RDF of the Adverse Outcome Pathway Database (AOP-DB) from the US EPA, who won the implementation challenge.

Provided by: Maastricht University

Type: Database / data source

Applicability domain: Toxicology, Bioinformatics Topic: Risk assessment, Information extraction

✓ For end-users

Category

▼ Service type

▼ User type

▼ Targeted users
▼ Filter Reset

Jaqpot API

Generate, store and share predictive statistical and machine learning models

Jaqpot is a user friendly web-based e-infrastructure containing many data analysis and modelling microservices integrated under harmonism d APIs. The Jaqpot infrastructure allows the user to build applications that preprocess data, compute ...

Provided by: National Technical University of Athens

Type: Analysis tool, Processing tool, Trained model, Model generation

tool, Model, Data mining tool, Service

Applicability domain: Computational modelling, Predictive toxicology

Topic: Biokinetics, Predictive modelling

- ✓ For developers
- ✓ For end-users

VikiPathways SPARQL Endpoint

WikiPathways was established to facilitate the contribution and maintenance of pathway information by the biology community. WikiPathways is an open, collaborative platform dedicated to the curation of biological pathways. WikiPathways ...

Provided by: Maastricht University

Type: Database / data source

Applicatility domain: Bioinformatics

Topic: Information extraction

Biological area: Acute toxicity, Carcinogenicity, Mutagenicity, Genotoxicity,

Skin sensitisation, Omics, Transcriptomics

For end-users

For developers

Jaqpot API

Generate, store and share predictive statistical and machine learning models

Jaqpot is a user-friendly web-based e-infrastructure containing many data analysis and modelling microservices integrated under harmonised APIs. The Jaqpot infrastructure allows the user to build applications that preprocess data, compute descriptors from raw data (such as electronic images), create, validate, store and share predictive machine learning models and generate reports in standard formats. Jaqpot has been developed by the Unit of Process Control and Informatics in the School of Chemical Engineering at the National Technical University of Athens.

API definition →

For developers

For end-users

Type: Service, Data mining tool, Model, Model generation tool, Trained model, Processing tool, Analysis tool

Categories: Knowledge bases, Processing and analysis, API Definitions for OpenRiskNet applications and data

Applicability domain: Computational modelling, Predictive toxicology

Topic: Predictive modelling, Biokinetics

Targeted industry: Chemicals, Nanotechnology

Targeted users: Risk assessors, Researchers, Students, Software Developers, Data managers

Relevant OpenRiskNet case studies:

ModelRX - Modelling for Prediction or Read Across

. RevK - Reverse dosimetry and PBPK prediction

Support contact: https://github.com/KinkyDesign/jaqpot-web/issues Documentation: https://github.com/KinkyDesign/jaqpot-web/

References and training materials:

- Chomenidis et al, 2017 (https://pubs.acs.org/doi/abs/10.1021/acs.jcim.7b00223)
- . Video: https://www.youtube.com/channel/UC-j4T6s5li4iMm76AAOiJ7w

Provided by: National Technical University of Athens

Contact: hsarimv@central.ntua.gr

Licence: GNU Lesser General Public License 3 (LGPLv3.0)

Login required: Yes

Implementation status: API documentation available (Swagger-OpenAPI v2), Containerised, Available as web service. Application programming interface available

Integration status: Integrated application

Service integration operations completed:

- Utilises the OpenRiskNet APIs to ensure that each service is accessible to our proposed interoperability layer.
- Is annotated according to the semantic interoperability layer concept using defined ontologies.
- ✓ Is containerised for easy deployment in virtual environments of OpenRiskNet instances.
- Has documented scientific and technical background.
- ✓ Is deployed into the OpenRiskNet reference environment.
- Is listed in the OpenRiskNet discovery services.
- ✓ Is listed in other central repositories like eInfraCentral, bio.tools and TeSS (ELIXIR).
- Provides legal and ethical statements on how the service can be used.

Resources & Training

RevK Pharmacokinetics OpenRiskNet Case study using Jaqpot web modelling platform

Philip Doganis 15 Oct 2018

→ Video

Model RX OpenRiskNet - Case study using Jaqpot web modelling

platform Philip Doganis

15 Oct 2018

www.openrisknet.org

Tutorial

Tutorial

Task	Services integrated*	1		2	3	4	5	6	7	8
	Squonk services for chemical property prediction	> /	S	quonl	k Con	ıp No	teboo	k		
	cpLogD	Σ	С	oLogi) con	fiden	e pre	dicto	r for l	ogD
	Modelling Web				х		х			
	CDK-Depict				х					
	Chemidconvert	>x	С	hemle	Con	/ert	Х	Х		X
4.1	eNanoMapper - nanomaterial database	$\sum x$	e	Nanol	Vlapp	er dat	abase			
4.1	FDA Estrogenic Activity Database	x		/	х	х	х	х		/
	MetPred	>x	M	etPre	d x	Х	Х	Х		
	LTKB	\geq	Ľ	TKB A	Pis		Х			
	ToxRefDB	\sqrt{x}			х					/
	ToxCast/Tox21 summary data	$\sum x$	E	delWe	eissD	ata (D	ata ex	cplore	er)	/
	Tox21 sample specific data	5×								
	TG-GATEs	×			х					
	Toxygates	Х			х					
	diXa (via BioStudies)	/								
4.2	Gene Expression Omnibus (GEO)					ise & data a		bla		
	ArrayExpress	,	III	Vitro	iiver	data a	avana	bie		
	EGA Beacon	>	E	GA B	eacor				Х	
	EGA Metadata	5	Е	GA M	etada	ta AP			Х	Х

x = full compliance, / = partly implemented

Task	Services integrated*	1	2	3	4	5	6	7	8
	BridgeDb	\sum_{X}	Bridge	Db id	lentif	er₃ma	pping	j serv	ice
	Data mining algorithms through Jaqpot	∑x	Jaqpo	t GUI	Х	Х	х	Х	/
	Data mining algorithms through JGU Weka	$\sum_{\mathbf{x}}$	JGU V	VEKA	RES1	Serv	ice	х	/
4.3	SCAIView Scientific Literature Database	\sum_{i}	SCAIV	iew	/				Х
	WikiPathways	>/	WikiP	athwa	ys [×] SF	ARQ	L end	point	
	AOP-Wiki	>/	AOP-V	Viki S	PARC	L en	dpoin	t	
	eNanoMapper - nanomaterial database	×	eNanc	Мăрр	er [×] Da	tabas	e ×	Х	
	Jenkins: ontology building and testing								
4.4	Ontology Lookup Service (OLS)	/	/	x	/				
	Ontology Annotation Services (BELIEF Text Mining)	/	/	х	/				
	Jaqpot processing and analysis services	$\sum x$	Jaqpo	t GUI	Х	Х	х	Х	/
4.5	CDK descriptor calculation service	>x	Jaqpo	t API	Х	Х	х	Х	/
4.5	PROAST and TCPL dose response modelling service	x							
	P450 SOM predictor	>x	P450	SOM I	oredic	tor	x		x
	WEKA REST Service	$\sum x$	JGU V	VEKA	RES	Serv	rice	Х	/
	Lazar Toxicity Predictions	>x	Lazar	Toxic	ity [×] Pr	edicti	ons		
4.6	Jaqpot predictive modelling services	$\sum_{\mathbf{x}}$	/	X	x	X	x	X	/
4.0	Jaqpot applicability domain services	∑x	Jaqpo	t GUI	X	х	х	Х	/
	Jaqpot PBPK modelling services	>x	Jaqpo	+ ADI	X	X	X	X	/
	httk package for PBPK modelling service	$\sum x$	Jaqpo	/	/	/	/		
	Squonk Computational Notebook	>/	Squor	k Coı	np No	otebo	ok		
4.7	Jupyter notebooks	\geq	Jupyte	r Not	eboo	K S X			
	Nextflow	\sum	Nextfl	pw ^x		Х			



^{*}New services from implementation challenge not yet included

Categories of services in ORN catalogue

Toxicology. **API Definitions** Omics database chemical for OpenRiskNet 4% properties applications and Visualisation and bioassay data and reporting databases 27% 11% 8% Knowledge Processing and bases 23% analysis 27%

There is an inconsistency between the categories in this figure and the ones in the tasks description

Task 4.1 Toxicology, Chemical Properties and Bioassay Databases

Task 4.2 Omics Databases

Task 4.3 Knowledge Bases and Data Mining

Task 4.4 Ontology Services

Task 4.5 Processing and Analysis

Task 4.6 Predictive Toxicology

Task 4.7 Workflows, Visualisation and Reporting



New services from the Implementation Challenge

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	<u> </u>	20	O O	*	*					
Holly Mortensen, US EPA - "AOP-DB (The Adverse Outcome Pathway Database)"				x	x					

Hyun Kil Shin, Korea Institute of Toxicology - "Daphnia magna nanotoxicity database" and

Virtual Screening of Metal Oxide Nanoparticles through Enalos InSilicoNano Platform" Igor Tetko, BIGCHEM GmbH - "OCHEM models", "OCHEM descriptors" and "OCHEM model

Antreas Afantitis, NovaMechanics Ltd - "Enalos InSilicoNano platform: an online decision support tool for the design and virtual screening of nanoparticles" and "A Risk Assessment Tool for the

"nano-QSAR to predict cytotoxicity of metal and metal oxide nanoparticles"

Johannes Kirchmair, Universität Hamburg - "FAst MEtabolizer (FAME)"

Urban Fagerholm, Prosilico - "Prosilico Human Clinical ADME/PK-Studio"

Rachael Skyner, Diamond Light Source Ltd. - "BruteReg" and "PySquonk"

Katy Wolstencroft, Leiden University (on behalf of EJP RD) - "ToxTargetLinks"

Benjamin Haibe-Kains, University Health Network - "ToxicoDB"

Matthias Timberlake, ToxPlanet - "ToxPlanet database"

development tool"

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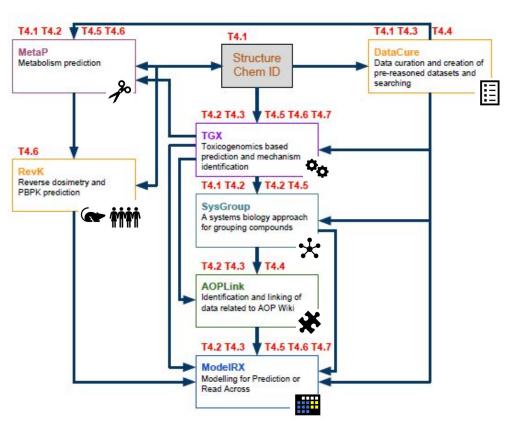
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Service integration in Case Studies

Example MetaP

Example TGX







Metabolism Prediction [MetaP]

CS leader: Daan Geerke (VU), Involved: UU, JGU, UHH

AIM: Integration of tools for site-of-metabolism (SOM) prediction and metabolite prediction

Ligand-based metabolite predictors (e.g. MetPred) and incorporate protein-structure and -dynamics based approaches to predict the site of metabolism (SOM) by **Cytochrome P450 (CYPs)**, which metabolize ~75% of the currently marketed drugs.

Objectives: Integration, comparison and combination of tools for metabolism prediction

- Ligand-based Site-Of-Metabolism (SOM) prediction using reaction SMARTS, circular fingerprints and/or atomic reactivities
- QSBR (quantitative-structure biotransformation relationship) modeling of microbial biotransformation
- Protein-structure and -dynamics based prediction of CYP450 isoform specific binding and SOMs
- Predicting probabilities for specific reaction type events

Risk Assessment Framework

Tier 0.1 (mol. structure), 1.5 (biokinetics), 1.6 (MoA)

Databases During method development, model calibration and validation we will use data from XMetDB and other open-access databases for drugs, xenobiotics and their respective metabolites.

XMetDB, SMARTcyp, ZINC, ChEMBL, EAWAG-BBD

Tools / APIs

- MetPred (UU)
- Metaprint2D & MetVap (UU)
- UM-PPS (JGU)
- enviPath (JGU)
- SMARTCyp (external service, integration by VU)
- Plasticity tools (VU)
- FAME (UHH; implementation challenge)

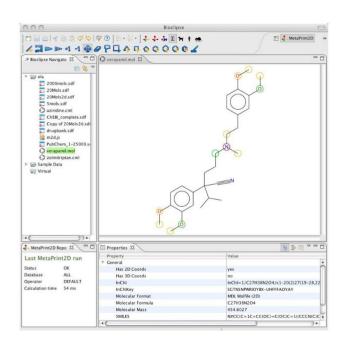
Service integration

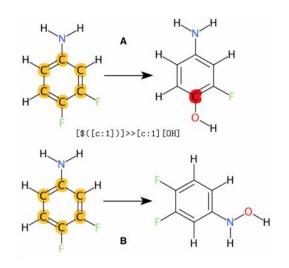
To facilitate combining metabolite prediction approaches and using MetaP outcomes as input for other predictors, we will take advantage of ongoing development in workflow management systems (Nextflow, Squonk, MDStudio) and we will explore integration into/with and use of these platforms. Once integrated the added value of multiple predictors will be subject of a pilot study on metabolite prediction..

openrisknet.org/e-infrastructure/development/case-studies/case-study-metap

MetPred

Predicts phase I metabolites: MetPred ranks most probable sites-of-metabolism (SOMs) and reaction types based on similar atom environments and ReactionSMARTS in annotated dataset [webservice; API available]



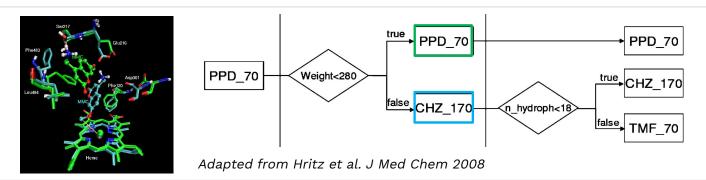


Carlsson et al. BMC Bioinformatics 2010 Arvidsson et al. Proc. Machine Learn. Res. 2017



Last years expansion of the toolbox

- **FAME 2.0**: SOM prediction (also for phase I, phase II or enzyme/isoform specific metabolism) from machine learning using (<)15 quantum and circular-environment based atomic descriptors [implementation challenge]
- **enviPath**: prediction of microbial biotransformation pathways and products using rules represented by SMIRKS
- **SMARTCyp**: SOM prediction for P450 metabolism based on fragment-mapping to pre-computed high-level QM data and atomic accessibility, extended with simple ligand-based pharmacophore rules for specific isoforms
- Protein-structure based predictors: plasticity models for docking into (flexible) P450 isoforms



Complementary tools, and we will explore added value of combined use for e.g. consensus prediction



o_o

Toxicogenomics based prediction and mechanism identification [TGX]

CS leader: Danyel Jennen (UM), Involved: UM, VU, CRG

AIM: To provide a transcriptomics-based hazard prediction model for identification of specific molecular initiating events (MIE)

The foreseen transcriptomics-based hazard prediction model will be applied based on:

- **(A) top-down** Creation of prediction models based on differentially regulated genes
- **(B) bottom-up** Using knowledge of stress response pathways to integrate data sets for their activation or inhibition (bottom-up approach).

The MIEs can include, but are not limited to:

(1) Genotoxicity (p53 activation), (2) Oxidative stress (Nrf2 activation), (3) Endoplasmic Reticulum Stress (unfolded protein response), (4) Dioxin-like activity (AhR receptor activation), (5) HIF1 alpha activation and (6) Nuclear receptor activation (e.g. for endocrine disruption).

Risk Assessment Framework

Tier 0.3-0.4 (data collection), 1.6 (MOA)

Databases

- diXa / BioStudies (UM)
- TG-GATEs
- EU-ToxRisk (nascent)
- HeCaToS (nascent)
- ArrayExpress / GEO

Tools / APIs

- top-down: Data normalisation tools, prediction tools such as Caret:
- bottom-up: ToxPi

Service integration

• Service integration will be needed for the omics databases; knowledge bases and data mining; processing and analysis.

Activities

- First top-down case study based on Magkoufoupolou et al 2012 paper
- Second top-down case study on meta-analysis for genotoxicity prediction in human, rat and mouse in vitro cell models

https://openrisknet.org/e-infrastructure/development/case-studies/case-study-tgx/



Example TGX (1) → top-down approach

Case study 1:

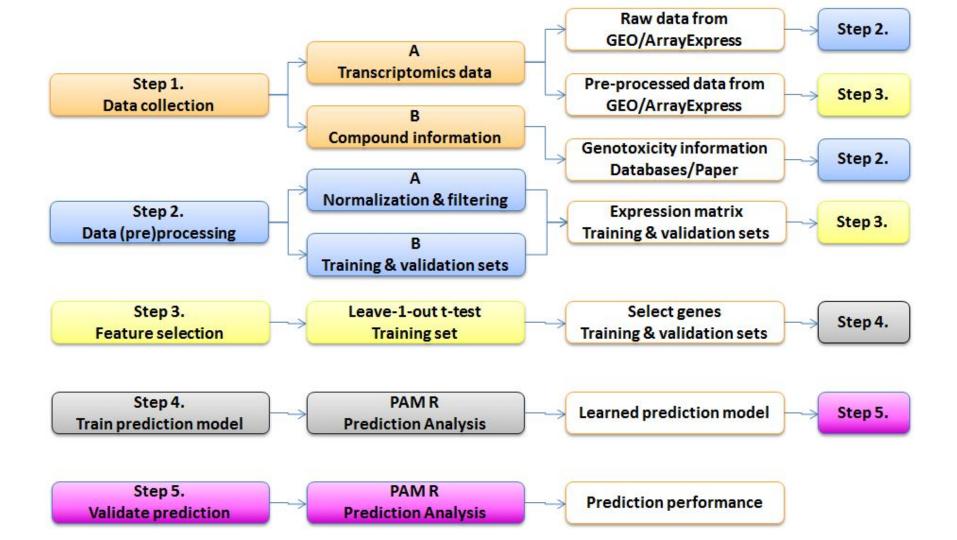
Create workflow based on Magkoufopoulou et al. 2012

Carcinogenesis vol.33 no.7 pp.1421–1429, 2012 doi:10.1093/carcin/bgs182 Advance Access Publication May 23, 2012

A transcriptomics-based in vitro assay for predicting chemical genotoxicity in vivo

C.Magkoufopoulou^{1,2}, S.M.H.Claessen¹, M.Tsamou¹, D.G. J.Jennen^{1,2}, J.C.S.Kleinjans^{1,2}, J.H.M.van Delft^{1,2,*}





Example TGX (2)

Current status

Workflow has been established in Snakemake and is available via Gitlab

Workflow is converted into NextFlow pipeline;

Converted into a generic workflow applicable to other datasets.

Next steps

Workflow will be containerized;

(Publication of approach)



Example TGX (3) → Generic workflow

- Data collection from GEO/ArrayExpress → API available
- Retrieve (geno)toxicity information
 - from databases
 - possible, but depends of required data
 - expert knowledge needed
 - from paper
 - difficult as presentation of information may vary

Fraunhofer

SCAL

- online pdf → difficult, because of format; suppl. data as Word, Excel, txt files → possible
- All other steps comprise of R-scripts → easy to adapt

→ data collection relies on available metadata, used format & ontologies

Collaboration with implementation challenge winners



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Investigate the pathways triggered by exposure to toxic substances (coming soon)



PDF: Table detection and -segmentation **Fraunhofer**

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Cortical inhibitory interneurons are, as well as PCs, a prominent target of cholinergic reuromodulation. The ways in which ACh modulates the dynamics of local interneurons have not been completely clarified yet, because the effects of BF cholinergic atmulation and bath application of cholinergic agreetes (Table 1) strongly depend on the inhibitory cell-type.

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Example TGX (4) → top-down approach

Case study 2:

Meta-analysis for genotoxicity prediction in human, rat and mouse *in vitro* cell models

In this case study transcriptomics data obtained from multiple data sources will be used to build a prediction model for *in vivo* genotoxicity.

A similar approach will be applied as in case study 1.

Preliminary results on the rat data have been presented at the ICCA-LRI workshop 2018, Ottawa, Canada Preliminary results on the human data have been presented at EUROTOX 2018, Brussels, Belgium



Example TGX (5) → top-down approach

The generic workflow will be applicable in this case study as well.

- Additional databases have been used, e.g. the diXa Data Warehouse
 → included in EBI's BioStudies → an API is available
- In vitro liver transcriptomics data from multiple human, rat & mouse cell models is available via Gitlab
- (Geno)toxicity data on all compounds has been collected
 - → valuable source for ToxicoDB

Other services from the implementation challenge can be incorporated.

→ ToxPlanet databases potentially can provide genotoxicity information



Deliverable 4.3

To do:

Update Deliverable 4.2 with the latest numbers:

- Add new services also from implementation services to table on slide
 11
- Adjust categories of services included in OpenRiskNet catalogue to the ones described in the tasks (see slide 16)
- Integrate (new) services with case studies



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P6 National Technical University Of Athens, Greece (NTUA)

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