Building a Collaborative Informatics Platform for Translational Research: An IMI Project Experience

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Living in the Era of BIG

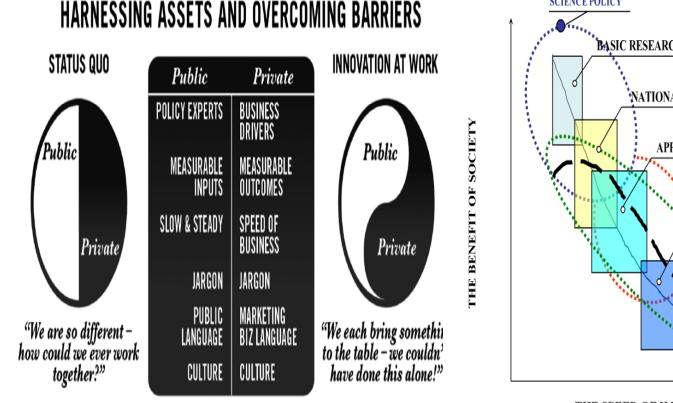
- Big Data : Massive amounts of information derived from dry /wet lab investigations, feasibility studies and clinical trials.
- Big Science: Research silos are evaporating with the merging of scientific methods. Traditional hypothesis-testing studies will couple with data-driven research.
- Big Collaboration : As evidence accumulates, personalized medicine will become a reality, and patient-specific cancer interventions will become available. Teams of disease specialists, researchers and bioinformaticians working in concert in a virtual frontier.

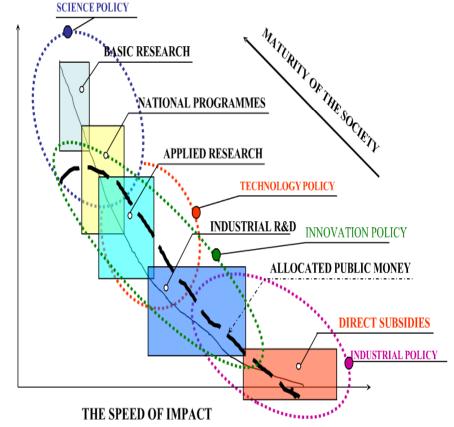


Collaboration Platform is the Key for Doing Big Science with Big Data



New Science Economy Model: Public-Private Partnership for Research

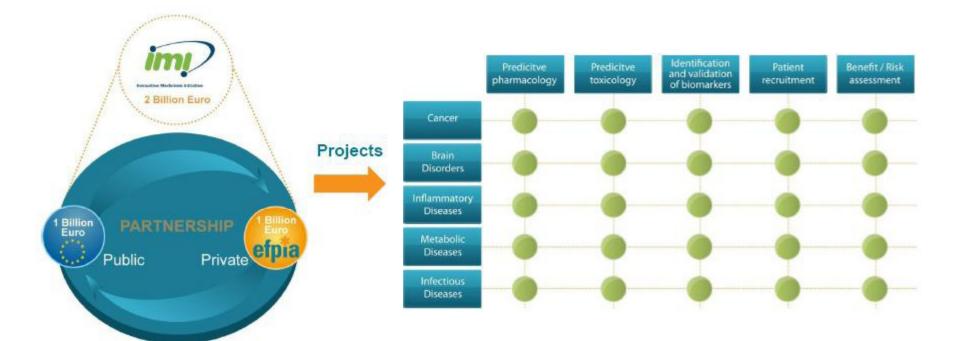




The Requirements for PPP-based Translational Research

- IT Infrastructure : hosted and shared by a community
- Data management: shared with configurable access control by various subgroups of a community
- Software : PaaS for development community
- Analysis : collaborative analysis
- Knowledge management: Dynamic integration of knowledge based on semantics

PPP Example : EU IMI



- New model for Public Private Partnership in Life Science
- Focus on Efficacy in 5 Disease Areas, Safety, Knowledge Management and Education & Training
- IMI projects address key pre-competitive bottlenecks identified by Pharma

U-BIOPRED Project: An IMI Project

Innovative Medicines Imitative (IMI)

- Worlds largest public private partnership
- 2 Billion Euro: 1 Billion from EU, 1 Billion from EFPIA

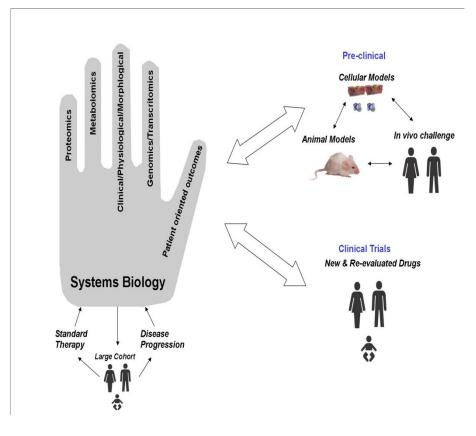
U-BIOPRED: Unbiased Biomarkers for predicting respiratory disease outcomes

 40 Party Collaboration between 10 Pharma & 30 Academic Medical Centres

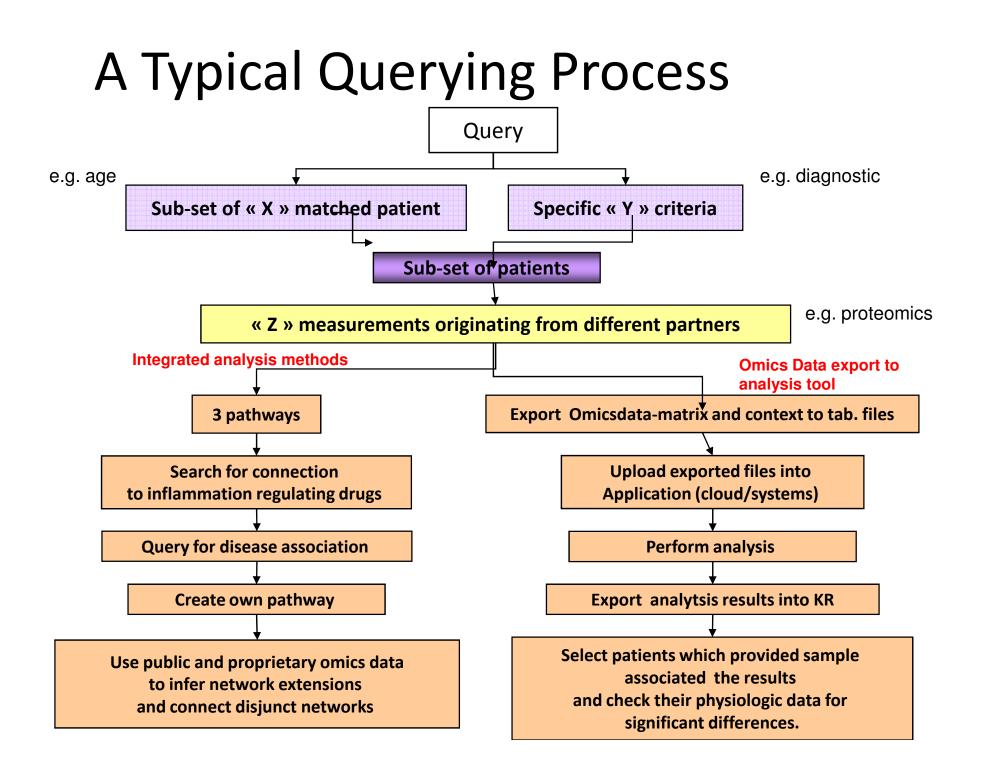
Knowledge Management Work Package

- Imperial Data Co-ordinator, JnJ TranSMART
- AZ, Roche, UCB, CNRS

UBIOPRED Knowledge Product : Handprints



- 1. Reaching international consensus on diagnostic criteria
- 2. Creating adult/pediatric cohorts and biobanks
- 3. Creating novel biology 'handprints' by combining molecular, histological, clinical and patient-reported data
- 4. Validating such 'handprints' in relation to exacerbations and disease progression
- 5. Refining the 'handprints' by using preclinical and human exacerbation models
- 6. Predicting efficacy of gold-standard and novel interventions
- Refining the diagnostic criteria and phenotypes
- 8. Establishing a platform for exchange, eduction and dissemination



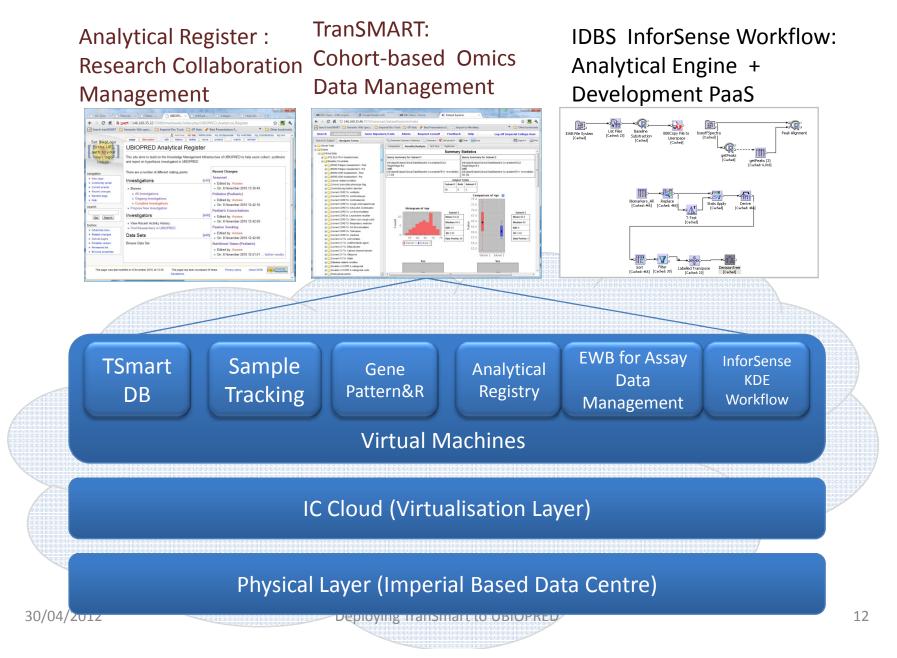
The Challenge in Building the KM for UBIOPRED

- The consortium formed as a loosely coupled virtual organisation
- Such a VO conducts highly collaborative and multidisciplinary scientific activities
- Data is generated by many people in the VO with a wide range
- of connected modalities
- Knowledge is build through an iterative knowledge production process where data need to be incrementally collected, flexibly integrated, systematically analysed and interactively reported
- Project has a period but knowledge need to be managed forever
- Very big task with very little money

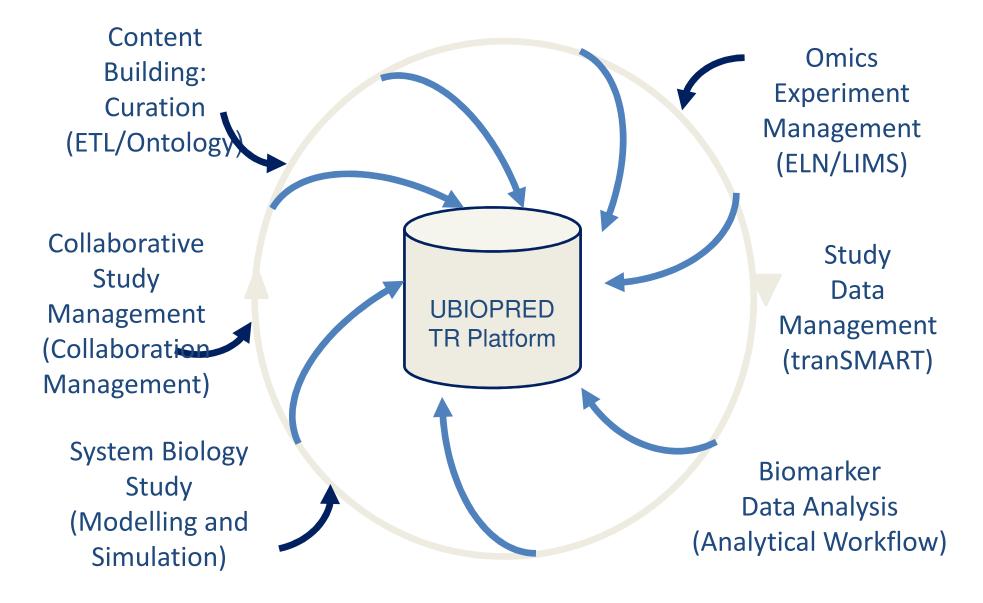
U-BIOPRED KM System Design Goal and KM Key Features

- Cohort-based information integration to support clinical driven integrative biomarker study
- Cloud based infrastructure to facilitate collaborative translational research
- An integrated framework supports the management of a collaborative knowledge production process (curation, analysis, content enhancement, reporting, modeling and simulation)
- A sustainable environment with longevity and total ownership : workflow-based PaaS for integrative analytics:
 - Curation ETL workbenches
 - Analytics workbenches
- A scalable platform adaptable for future science/technology development (such as NGS technology; medical image et.al)

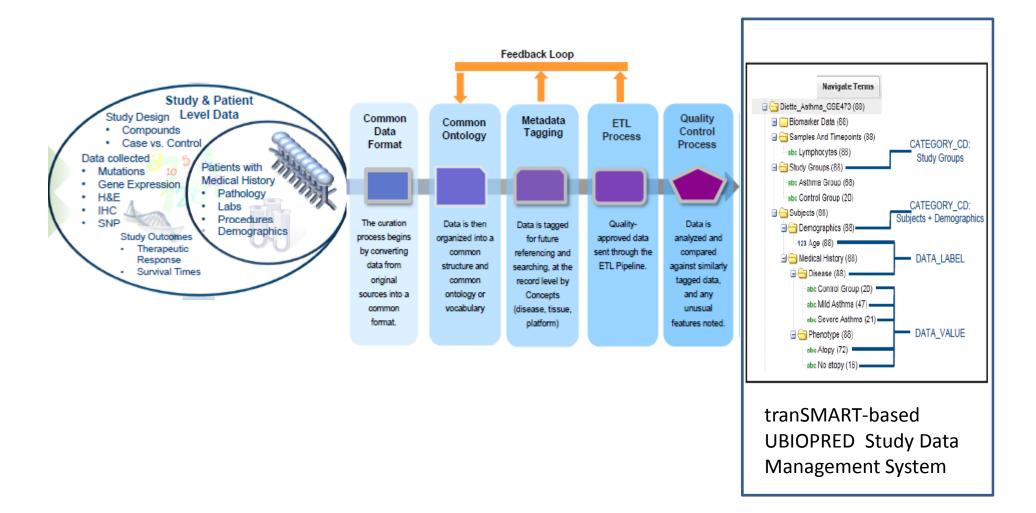
UBIOPRED Collaborative TR Platform



UBIOPRED TR Platform Components

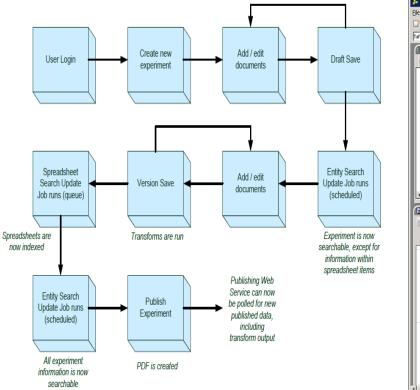


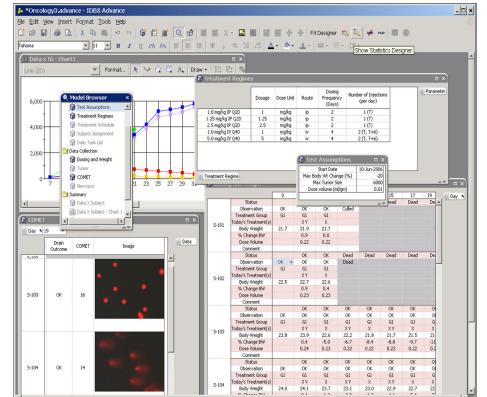
Curation: Building Study Contents and Background Knowledge



Omics Experiment Management

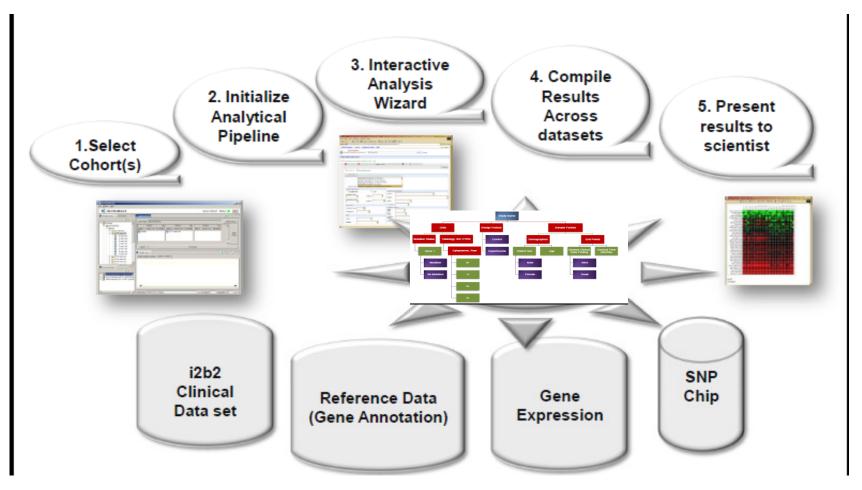
Omics experiments (Proteomics, lipidomics experiments (WP7) and pre-clinical study (WP6) are managed with EWB of IDBS





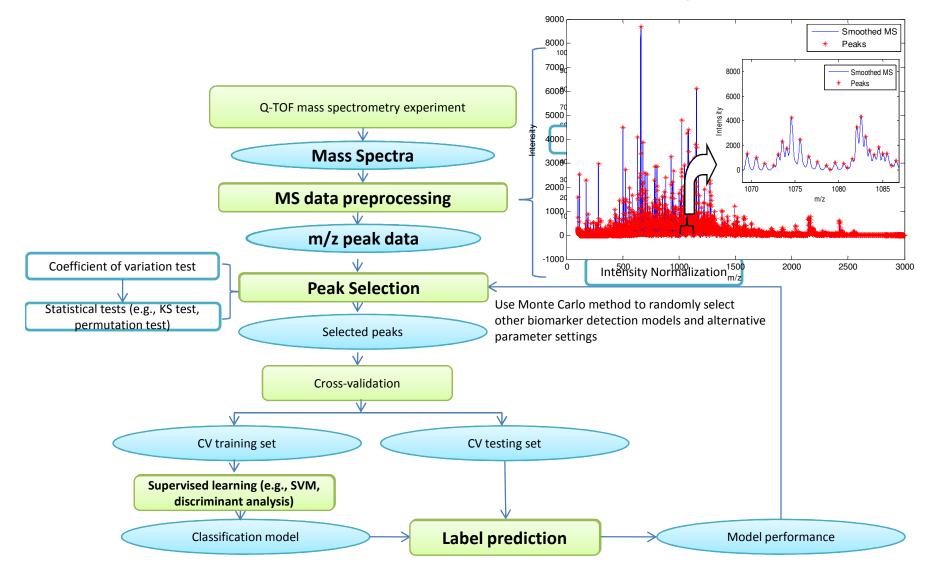
Study Data Management

Study oriented curated data together with patient information are integrated and warehoused in tranSMART for analysis (WP8)

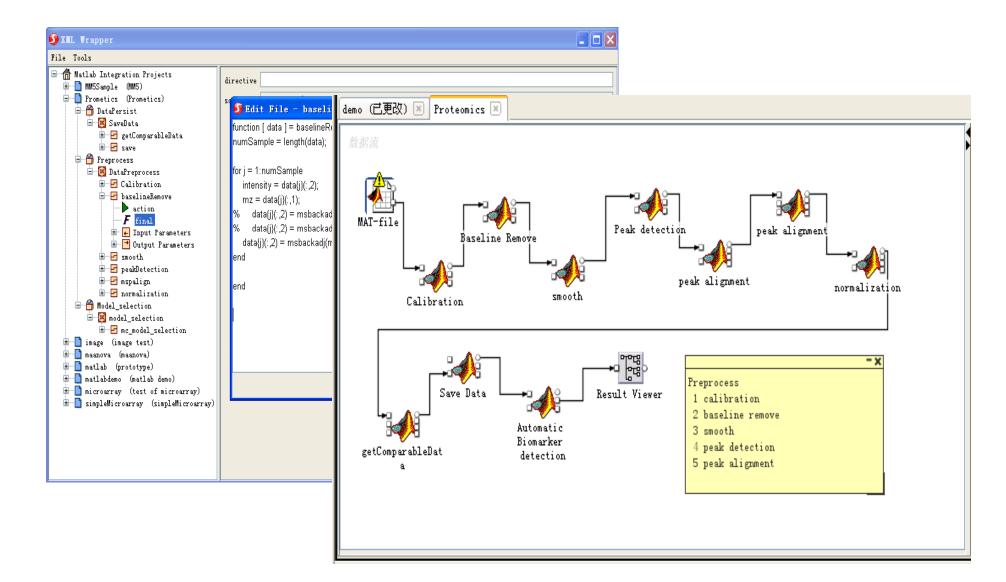


From John Shon et.al tranSMART , AMIA TBI 2012

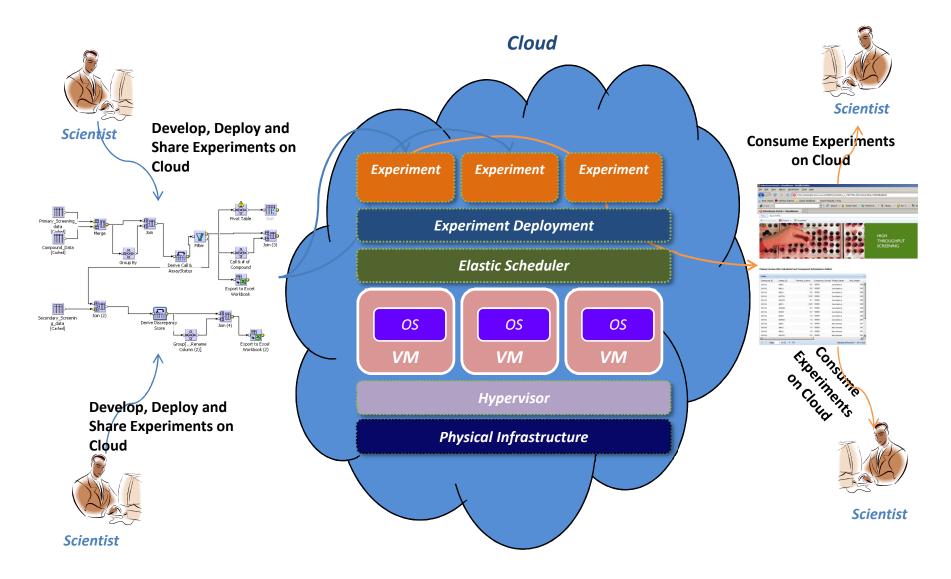
Workflow-based Analytics: A Proteomics Example



Workflows in InforSense

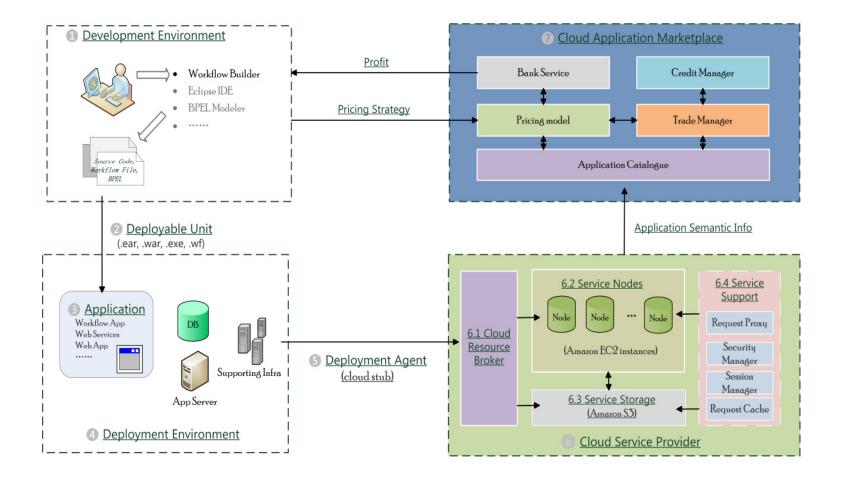


Workflow Deployed as Cloud Applications



A Development Cycle of Cloud Application Building via Workflow

Current development/deployment paradigm + Elasticity + Economic Model



Analytical Register: Enables Collaborative Knowledge Management



A Home

Studies

A Cohorts

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Toolbox

X Admin Tools

Procedures

U-BIOPRED Analytical Register

Foswiki > UBIOPRED Web > WebHome

Hello Michelle Osmond Log Out

Home

Welcome to the Analytical Register.

Recent Updates

Work Packages Knowledge Management User Manual (Michelle Osmond, 6 hours and 58 minutes ago) Validate ECLIPSE microarray data loaded into tranSMART (Michelle Osmond, 1 week, 4 days ago) Investigations Minimunopathology phenotype as part of handprint (Michelle Osmond, 1 week, 4 days ago) Transmart Smoke Test (Michelle Osmond, 1 week, 6 days ago) Researchers Organisations Pre-processing raw Affymetrix microarray data for Analysis (Michelle Osmond, 1 week, 6 days ago) Debrecen RMA (Michelle Osmond, 1 week, 6 days ago) Influence of gender (Michelle Osmond, 2 weeks, 1 day ago) Recent Updates Influence of pollution (postal code) (Michelle Osmond, 2 weeks, 1 day ago) TranSMART 2 Adult onset versus childhood onset (Michelle Osmond, 2 weeks, 1 day ago) Eeedback/Bugs Create New Topic Upper vs lower airways phenotypes (Michelle Osmond, 2 weeks, 1 day ago)

more.

Pages for you

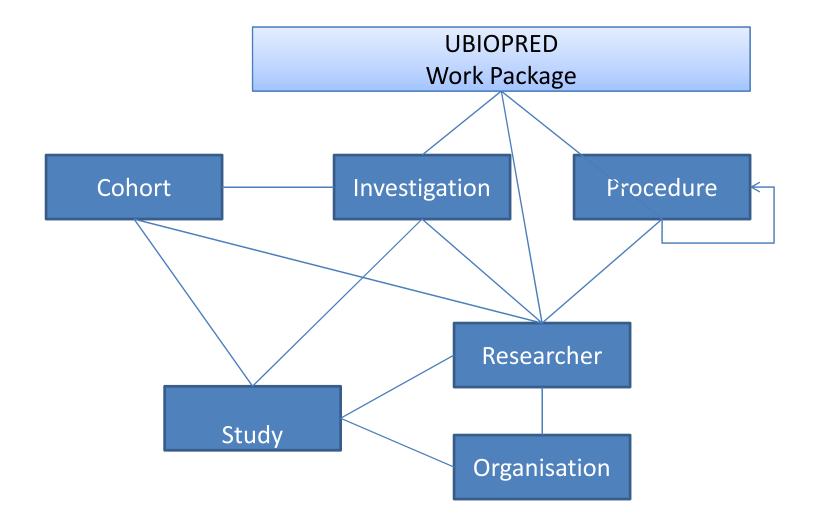
Procedures:

- Knowledge Management User Manual
- Transmart Smoke Test

Cohorts:

Edit Attach

Mapping Research Collaboration in UBIOPRED



Analytical Register: A Study View

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	About	study will collect various data types to s	support the generation of the Handprint. Ea	ich data set is used	to generate an individual fingerprint that in turn will be combined into a	Provider:	U-BIOPRED Consortium (UBIOPRED)
Transmart Studies	specific handprint.					Owner:	Manohara Batuwitage (LOIC)
Vork Packages	Data avai	lable				Contacts:	Anthony Rowe (JNJ)
Cohorts Investigations Procedures Researchers	Data Class	Assay/Data Source	Cell Types Number of Samples	Contact		Relevant Disease Areas:	Asthma
esearchers rganisations	Clinical	ECRF		Kerry Dyson			Clinical Transcriptomics
ecent Updates	Clinical	Patient Reported Outcomes		Kerry Dyson			Proteomics Lipidomics
anSMART 🖉	Clinical	Patient Diaries	-	Florian Singer WP7- LOIC		collected:	5
edback/Bugs	Transcriptomics Proteomics	Human Genome U133 Plus 2.0 Array Unselective ESI		Paul Skipp		Number of	Histology
Create New Topic	Proteomics	MSe		Paul Skipp		Patients:	
	Lipidomics			Tony Postle		Date	
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	Metagenomics			Peter Howarth			
	СТ	AirProm	-	Sumit Gupta			

Susan Wilson

Work Packages in this study:

Waiting for Agreement

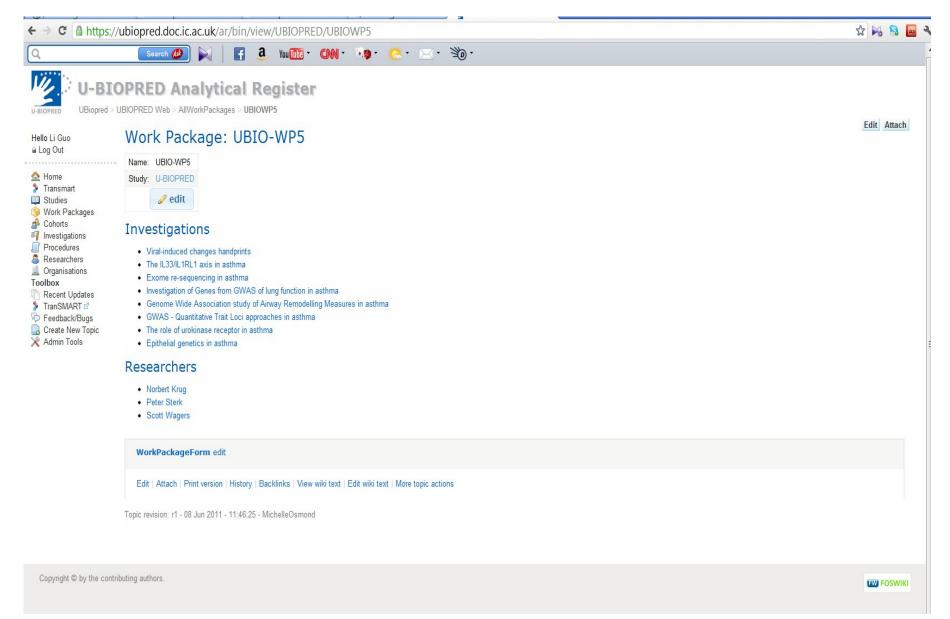
Broncoscopy

UBIO-WP10

Histology

- UBIO-WP2
- UBIO-WP3
- UBIO-WP4
- UBIO-WP5
- UBIO-WP6
- UBIO-WP7
- UBIO-WP8
- UBIO-WP9

Analytical Register: Work Package View



Analytical Register: A Cohort View

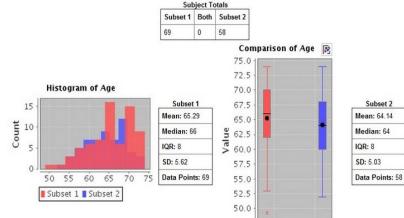
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ate New Topic	Identifying severe asthmatics with irreversible airflow limitation (as defined by TENOR	ECLIPSE	Michelle Osmond (LOIC)	191	1787922 🖙	
min Tools	FEV1 vs Exacerbation Rate	ECLIPSE	Anthony Rowe (JNJ)	148	1787925 🖾	
	COPD Patients for Clustering Analysis	ECLIPSE	Manohara Batuwitage (LOIC)	148	1787928 🖙	
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	O Add new cohort					
	Edit Attach Print version History Backlinks View wiki text Edit wiki text	More topic actions				
	Topic revision: r9 - 04 Apr 2011 - 15:59:09 - MichelleOsmond					

Analytical Register: Interfacing to Cohort Selection

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Analytical Register – Cohort View





Analytical Register: An Investigation View

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		Epithelial genetics in asthma Proposed; Initiator: Dominick Shaw Contributors: Dominick Shaw 16 Apr 2012 - 10:38 Background: GWAS data in asthma suggests that multiple genes of relevance to airway epithelial function are potentially altered. These findings require the characterisation of cellular responses in carriers and r Aires: To identify carriers and non carriers of relevant risk alleles and characterise primary bronchial epithelial cell functions relevant to these targets e.g. SMAD3 SNPs and TGFE1 signalling. genotypes U-BIOPRED UBIO-WP3, UBIO-WP4, UBIO-WP5, UBIO-WP6, UBIO-WP7	ton-carriers of relevant risk alleles.
		GWAS - Quantitative Trait Loci approaches in asthma Proposed; Initiator: Dominick Shaw Contributors: Dominick Shaw 16 Apr 2012 - 10:35 Background: Data relating genetic polymorphism with mRNA expression in asthma subjects is sparse. With advances in genomics approaches it is now possible to generate a GWAS SNP dataset and global mRNL cell. These data will potentially aid the translation of recent findings from asthma GWAS and potentially take our understanding of asthma in new directions. Aims: To complete a GWAS and quantify gene expression in all subjects e.g. Affymetrix array from a) lung tissue, b) bronchial epithelial cells, c) airway fibroblasts, d) airway smooth muscle cells and e) peripheral blood mononuclear or ECLIPSE, U-BIOPRED UBIO-WP3, UBIO-WP4, UBIO-WP6	
		Genome Wide Association study of Airway Remodelling Measures in asthma Proposed; Initiator: Dominick Shaw Contributors: Dominick Shaw 16 Apr 2012 - 10:34 Background: Structural alterations termed "airway remodelling" occur in asthma and the extent of remodelling is variable. Airway remodelling is a characterised by; smooth muscle hypertrophy/hyperplasia, sub-ep thjckening, increased extracellular matrix deposition, angiogenesis and more recently alterations in epithelial functions have been identified including metaplasia and goblet cell hyperplasia. The mechanisms underlying airway remo	

Analytical Register: Investigation Drill Down

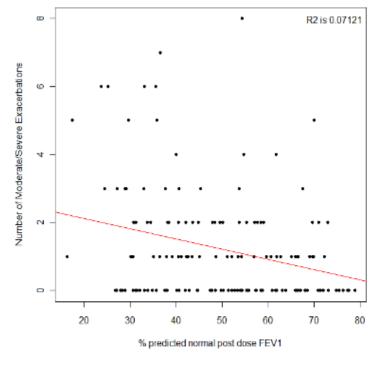
	DPRED Analytical Register BIOPRED Web > AllInvestigations > Investigation_0002 Investigation: Is there a relationship Exacerbation Rate and FEV-1 in COPI		
Home Studies	Table of Contents	Owner:	Manohara Batuwitage (LOIC)
Work Packages Cohorts Investigations Procedures Researchers Organisations	 ↓ Research Hypothesis ↓ Cohorts Used ↓ Method and Results ↓ Conclusions ↓ Comments 	Contributors:	Anthony Rowe (LOIC), Manohara Batuwitage (LOIC)
		Status:	Ongoing
		Categories:	Methodology
oolbox ☐ Recent Updates ☐ TranSMART ☑ ☐ Feedback/Bugs ☐ Create New Topic ✔ Admin Tools	Research Hypothesis A core dogma of COPD research is that as FEV-1 decreases the number of	Studies used:	ECLIPSE
	exacerbations a COPD sufferer experiences will increase. Or to put simply it is expected that exacerbations will increase as lung function deteriorates.		
	This study investigates whether this correlation exists in the Eclipse study data.		
	• FEV1 vs Exacerbation Rate (TranSMART: 1787925 ☑)		
	O Add link to cohort		

Analytical Register Further Drill Down: Method

Method and Results

Based on the ECLIPSE cohort of patients we fitted linear models between the % predicted normal post-dose FEV1 score and the exacerbation rate that patients had in Years 1,2 & 3 of the ECLIPSE study. Selection of the patient data was conducted through TranSMART and the patient data extracted and analysed using the R platform. (The R Code for this analysis is attached here)

Year 1 - FEV1 VS Exacerbation Rate (R2 = 0.07121):



FEV1 Vs Exacerbation Rate (Year1)

Year 2 - FEV1 VS Exacerbation Rate (R2 = 0.06442):

Analytical Register: Interfacing to Sample Tracking

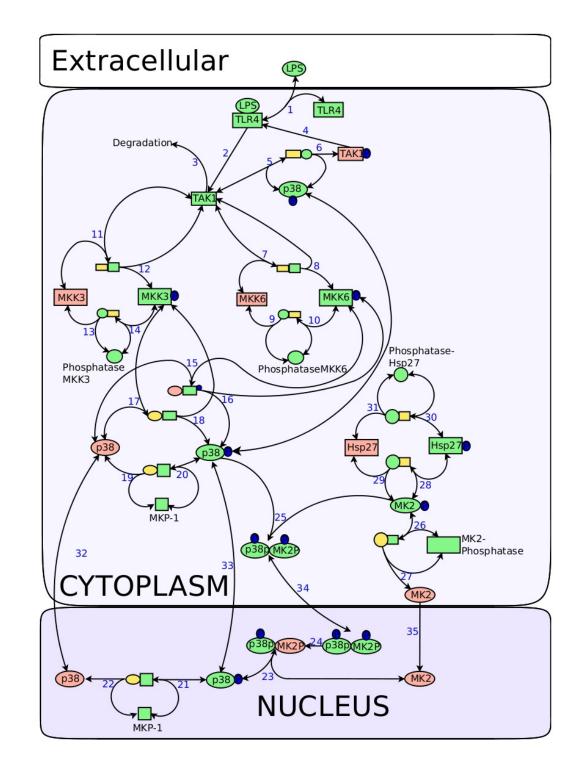
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Analytical Register: Fully Integrated with TranSMART

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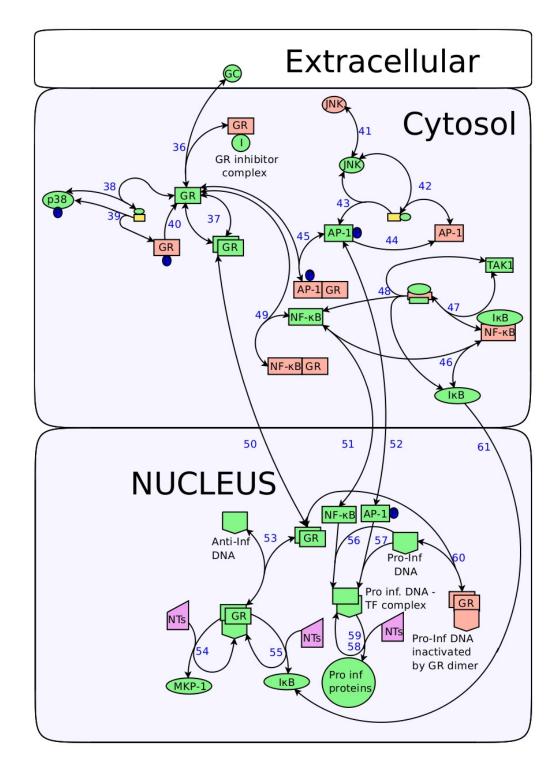
UBIOPRED System Biology Study

 We have developed p38 pathway model in SBML and perform simulation throughput MATLAB.



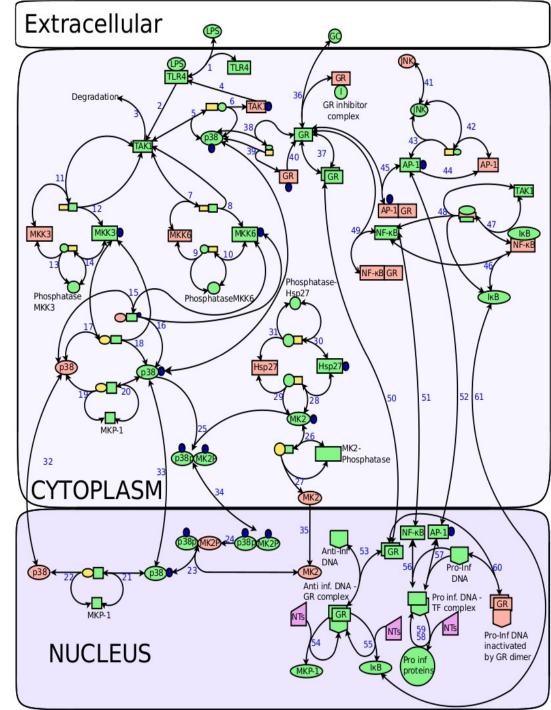
UBIOPRED System Biology Study

2. We have proposed a novel glucocorticoid signalling pathway model in SBML.

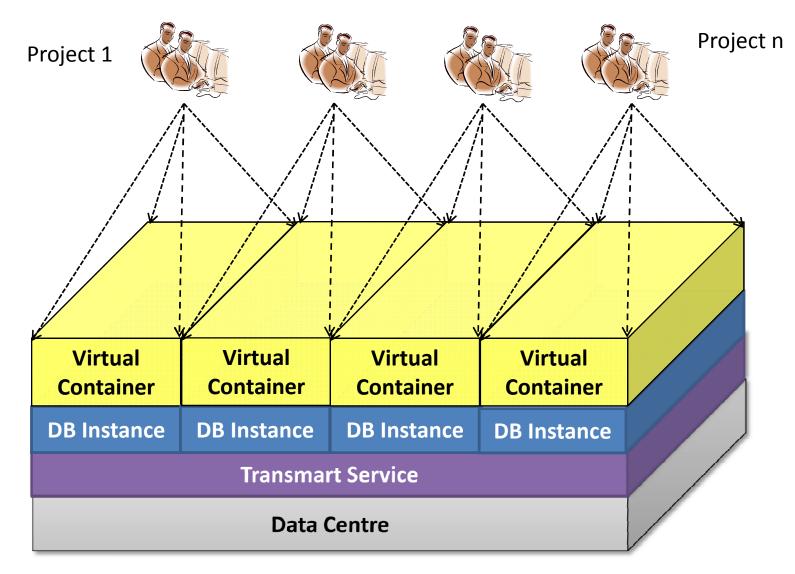


UBIOPRED System Biology Study

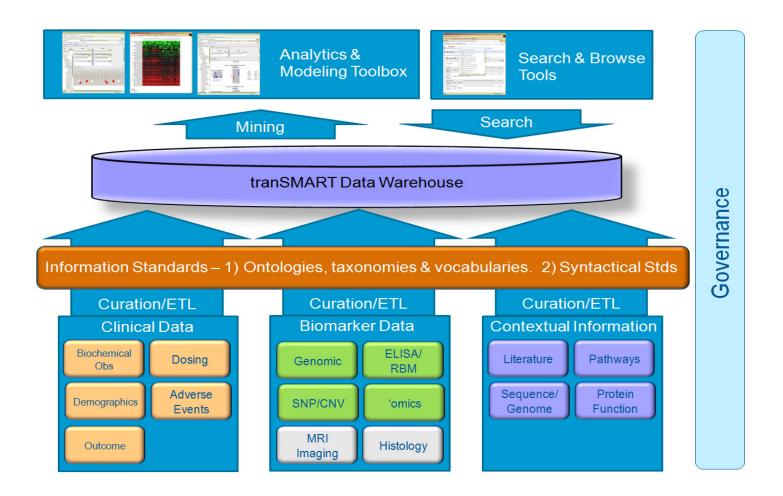
- 3. We have proposed some hypotheses to suggest possible crosstalk between GC and p38 pathways.
- 4. We then construct the integrated pathway model in SBML.
- 5. Test the stability of this integrated model.



Extending UBIOPRED to Support Multiple Projects



eTRIKS : European translational research and knowledge management services



Conclusion: the end of the begining

- UBIOPRED knowledge management system supports cross-institutional large scale translational research
- UBIOPRED knowledge management system support the entire knowledge production process
- For PPP-based TR projects, collaborative research support in a VO environment is circuital
- Modern technology such as cloud and workflow provide the technical foundation for its implementation
- The development is moving forward to support IMI translational projects in general by eTRIKS project