10 YEARS OF BREAKTHROUGHS A HEALTHIER FUTURE

eTOX

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Developing predictive *in silico* models for liver toxicity endpoints from *in vivo* histopathology data

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Facts & Figures

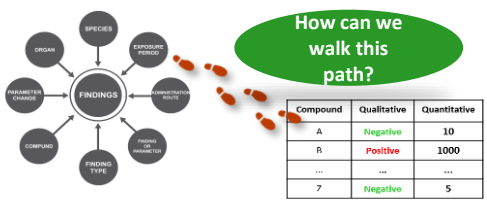
Start date:	01/01/2010
End date:	31/12/2016
Contributions	
IMI funding:	6,910,018 €
EFPIA in kind:	10,157,590 €
Other:	1 719 500 €
Total Cost:	18,877,109 €
Project website:	www.etoxproject.eu

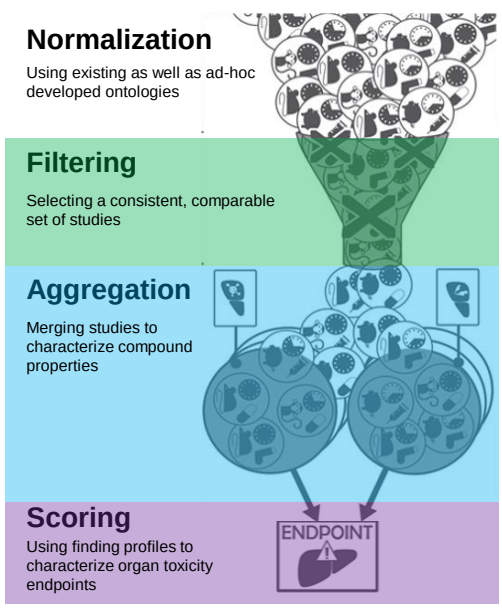
Social media: www.youtube.com/watch?v=fMWpDUaOdNc

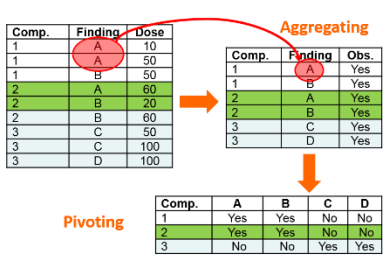
Challenge

- The **eTOX** project compiled a collection of nearly 9000 of such studies.
- In this work we describe how these collected data can be exploited for the development of predictive models for *in vivo* toxicity endpoints.

Approach & Methodology





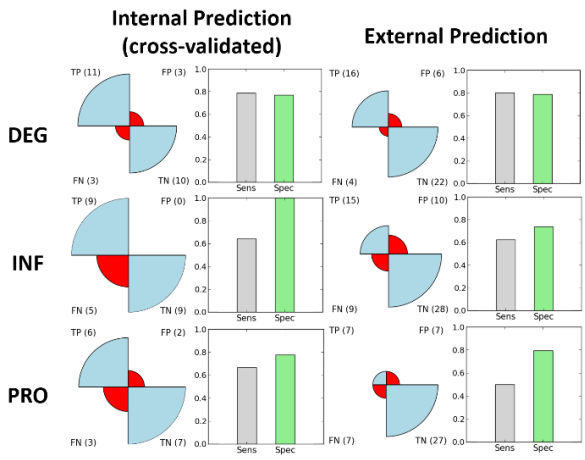


Results

Distribution of qualitative hepatotoxicity scorings.

Liver in vivo Endpoint	Positive compounds	Negative compounds
Degeneration (DEG)	164	168
Inflamatory (INF)	94	164
Non-neoplasic Proliferative lesions (PRO)	82	164

Representation of the confusion matrix, sensitivity and specificity for the best qualitative models obtained using conformal Random Forest Classifier.



Quality parameters of conformal model predictions.

Endpoint	Internal prediction (cross-validation)		External prediction	
	Coverage	MCC	Coverage	MCC
DEG	0.47	0.55	0.48	0.58
INF	0.74	0.64	0.81	0.44
PRO	0.64	0.45	0.65	0.29

In general, the quality of the models is acceptable, if we consider the complexity of the *in vivo* endpoints, representing many different mechanisms of liver toxicity.

Value of IMI collaboration

- The results shown here are only an example of how the results of the **eTOX** project (the **eTOX** database and **eTOX**sys) are being exploited for practical purposes.
- The **eTOX** database represents a successful example of precompetitive sharing of information between 13 pharmaceutical companies, made possible thanks to the public-private partnership IMI project.

Impact & take home message

- The information present in RDT reports generated for regulatory purposes can be transformed to obtain data amenable for developing predictive models.
- These models exemplify the practical use of the *in vivo data* collected by the **eTOX** project.
- Precompetitive collaboration can produce valuables resources which can be exploited to obtaining safer and more effective drugs, in a faster way.

imi innovative medicines initiative efpia

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