

3rd Annual Predictive Toxicology

half day interactive pre-conference workshop

Tox IVIVE - inter-individual variability matters!

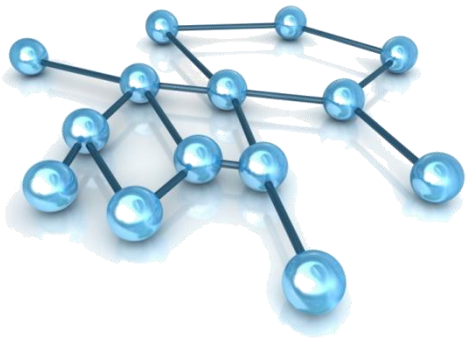
ToxComp platform – future development

Sebastian Polak



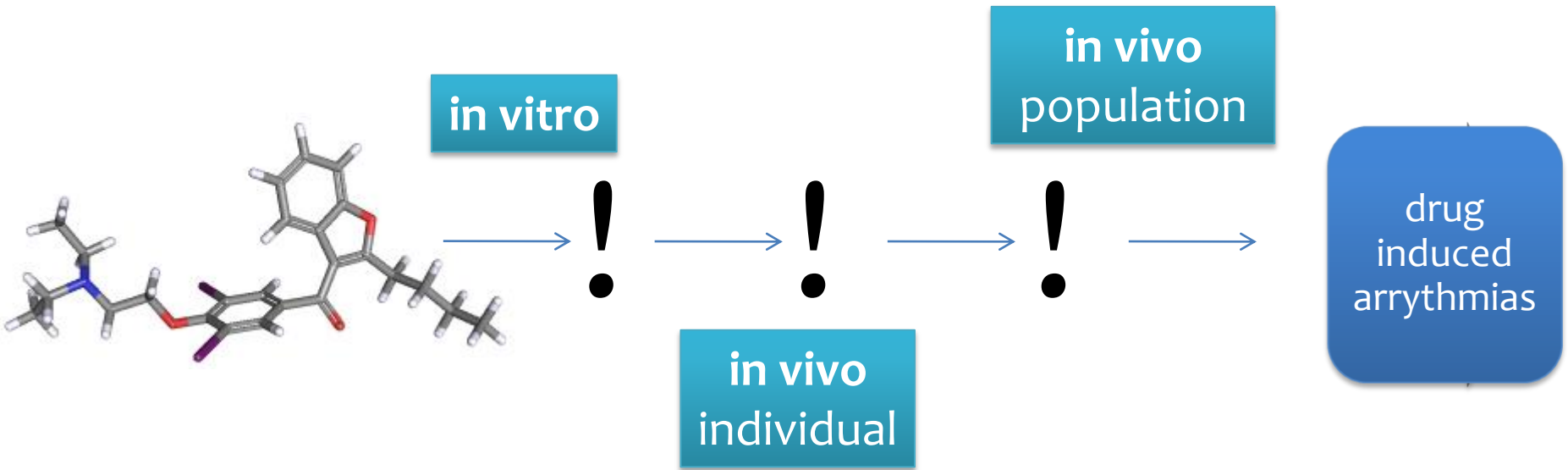
Unit of Pharmacoepidemiology and
Pharmacoeconomics
Jagiellonian University Medical College

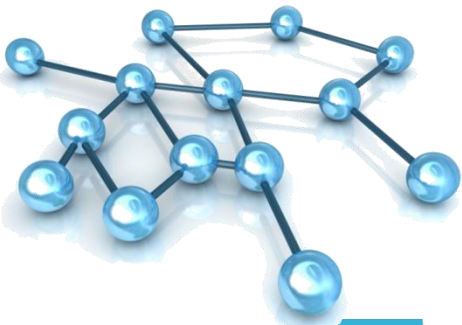




proarrhythmic potency assessment

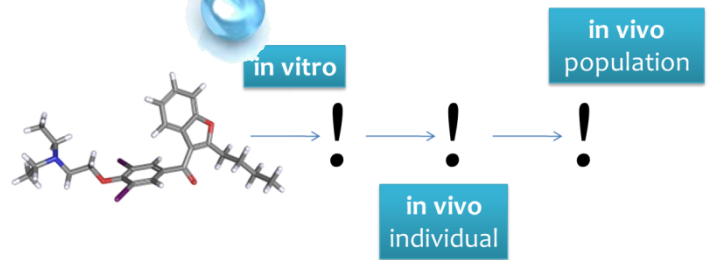
in silico – in vitro – in vivo extrapolation





proarrhythmic potency assessment

in silico – in vitro – in vivo extrapolation



MODULE 4
ADME IVIVE

MODULE 1

hERG in vitro

hERG in silico

MODULE 2

other ion channels in vitro

other ion channels in silico

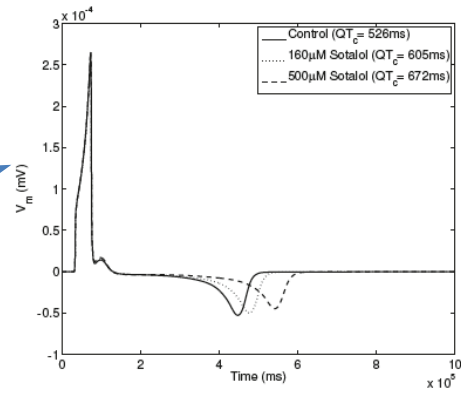
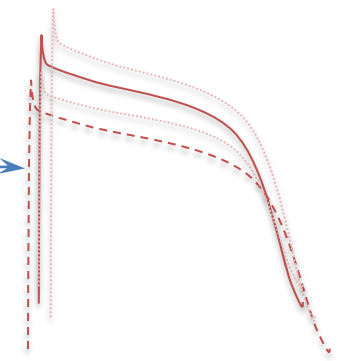
MODULE 3
HEART VENTRICULAR CELL MODEL

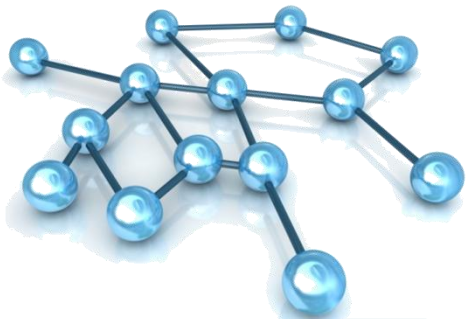
DEMOGRAPHIC & PHYSIOLOGICAL & GENETIC DATA

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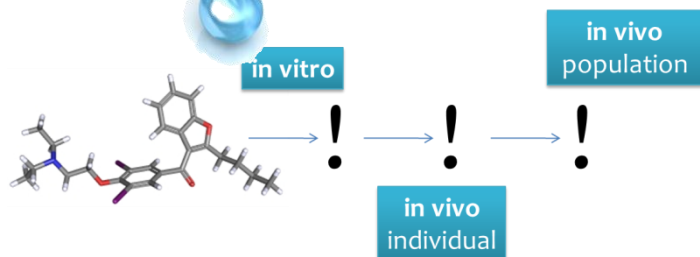
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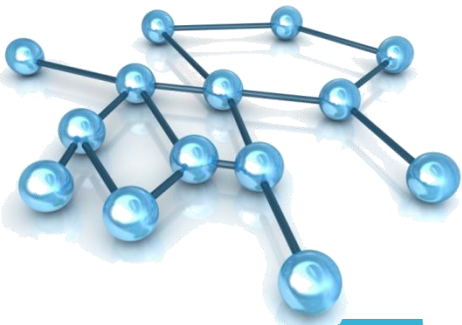
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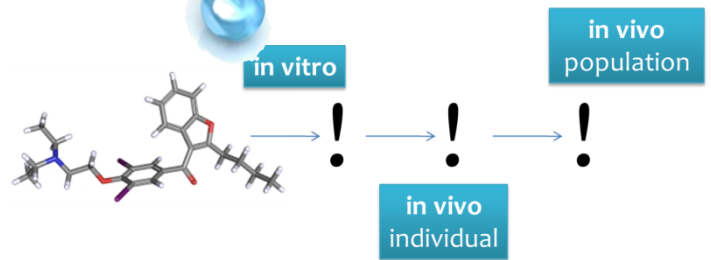
- **INa**
 - ongoing project
 - less in vitro data than for hERG
 - unacceptable error so far
- **ICa**
 - much less in vitro data than for hERG
 - modeling is connected with a risk of substantial error

other ion
channels *in
silico*



proarrhythmic potency assessment

in silico – in vitro – in vivo extrapolation



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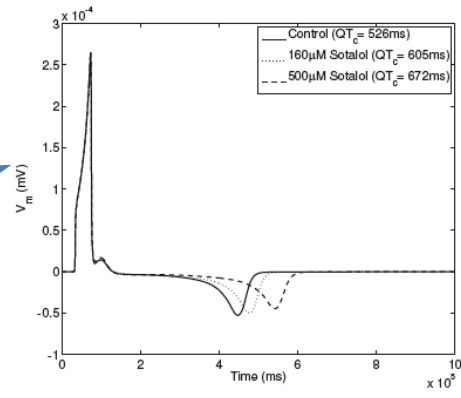
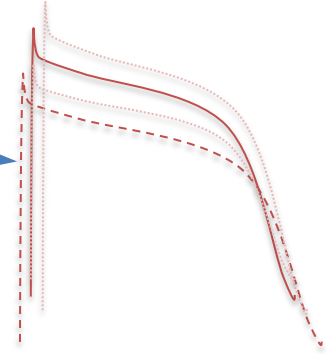
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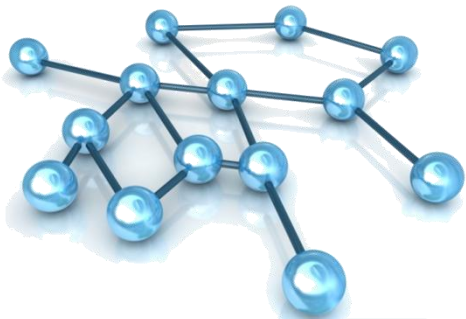
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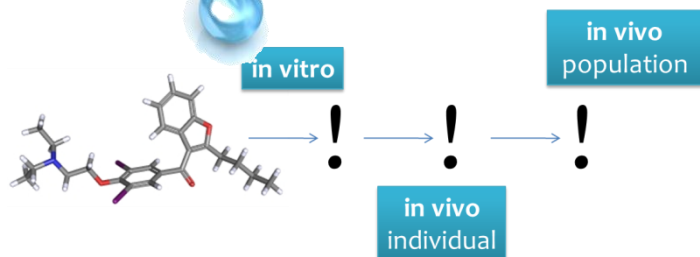
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proarrhythmic potency assessment

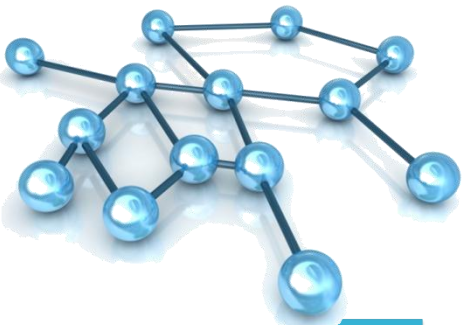
in silico – in vitro – in vivo extrapolation



- **physiological ionic serum concentration**
 - ongoing project
 - model development based on the clinical data from healthy volunteers studies
- **genetic variability**
 - pathological genetic variants

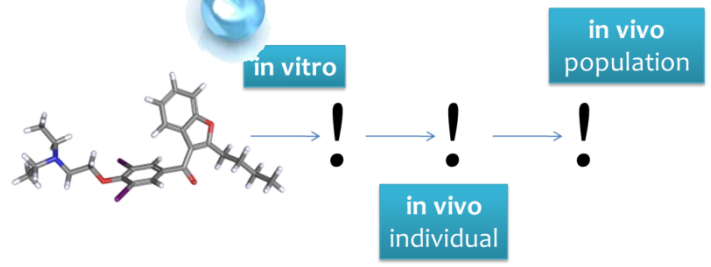
- **population definition flexibility**

DEMOGRAPHIC
&
PHYSIOLOGICAL
&
GENETIC DATA



proarrhythmic potency assessment

in silico – in vitro – in vivo extrapolation



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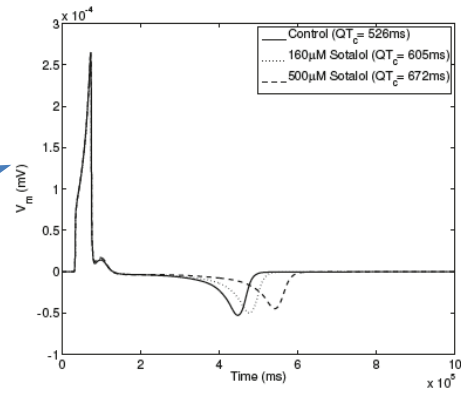
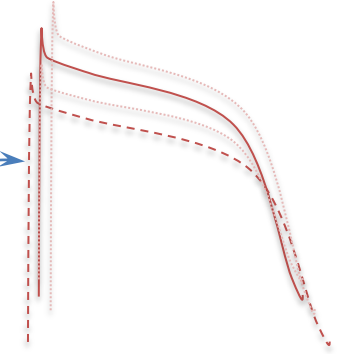
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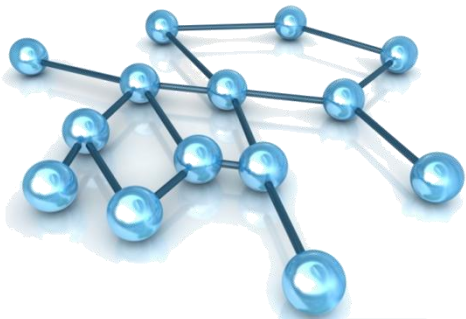
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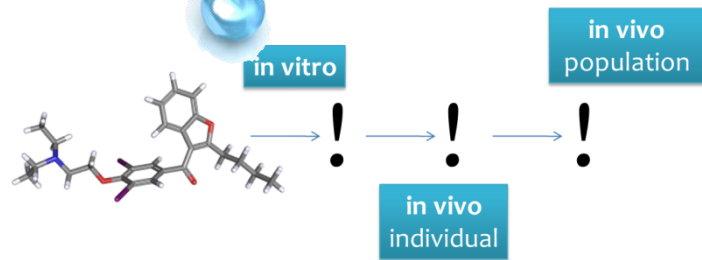
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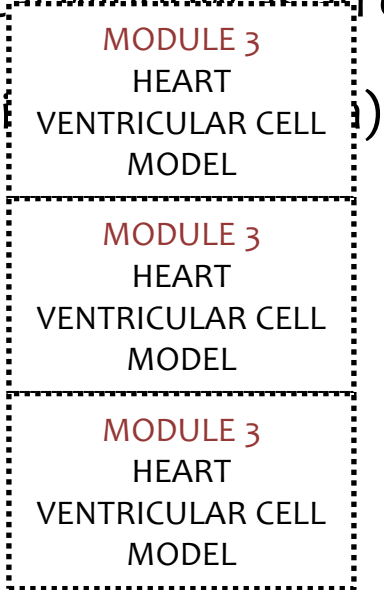


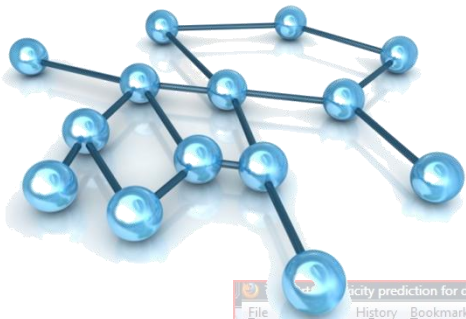
proarrhythmic potency assessment

in silico – in vitro – in vivo extrapolation



- **electromechanical coupling**
 - ongoing project
 - electro-mechanical window as an output
 - problem – validation





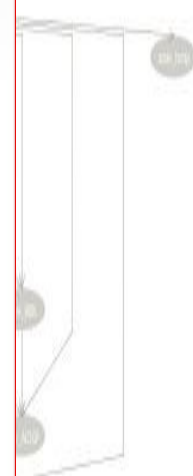
proarrhythmic potency *in silico*

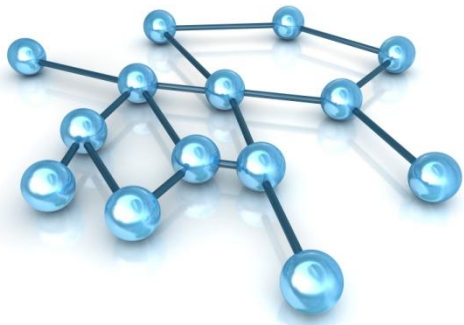
ToxComp.net

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- A
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more information can be found at the

www.tox-portal.net





acknowledgements

team

Barbara Wiśniowska PhD

Aleksander Mendyk PhD

Miłosz Polak

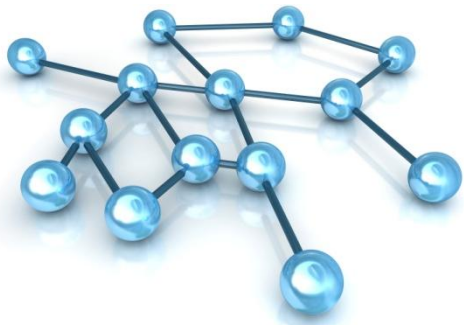
Kamil Fijorek

Anna Glinka

Małgorzata Kozłowska



project financed by the **Polish National Center for Research and Development** LIDER project number LIDER/02/187/L-1/09



acknowledgements

contact

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Faculty of Pharmacy

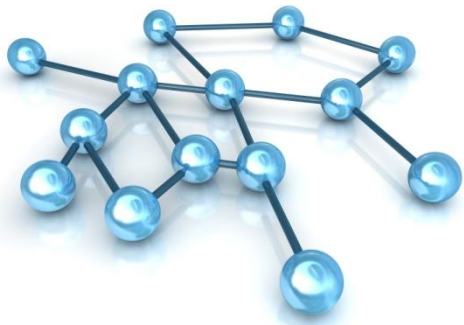
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THANK YOU



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