[#30] Anna Kreutz

Quantitating population toxicokinetic variability utilizing recombinant enzyme-specific clearance rates

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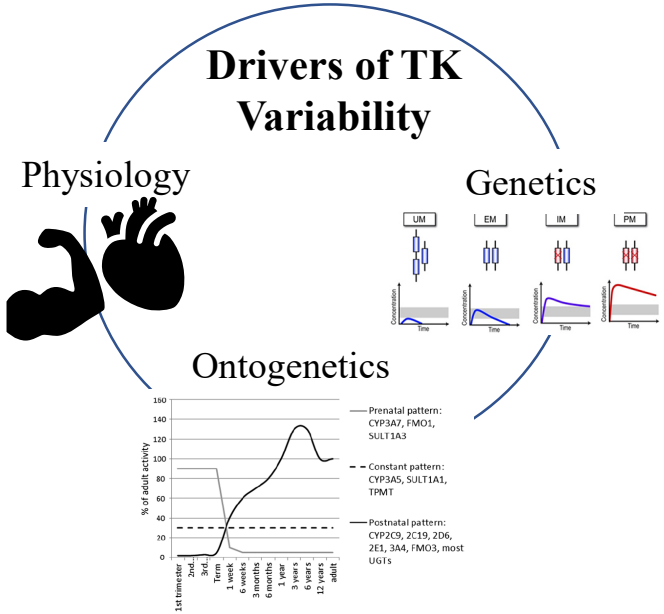
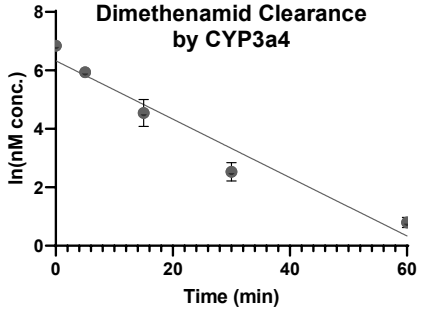
Background & Methods

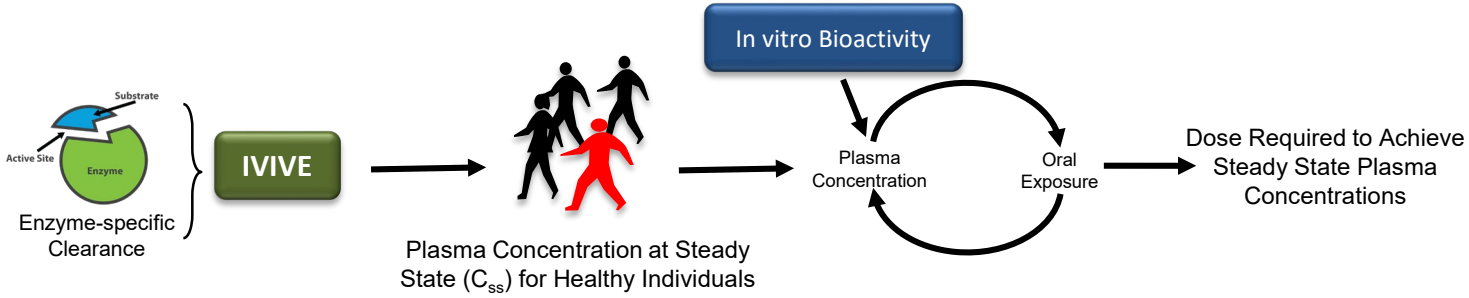
- Identical external chemical exposures may yield distinct systemic concentrations & health impacts



- Clearance rates generated for recombinant isozymes



- IVIVE used to predict in vivo exposures



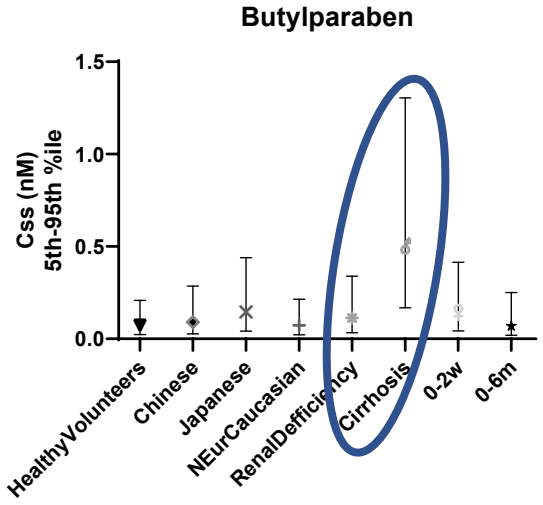
Preliminary Results

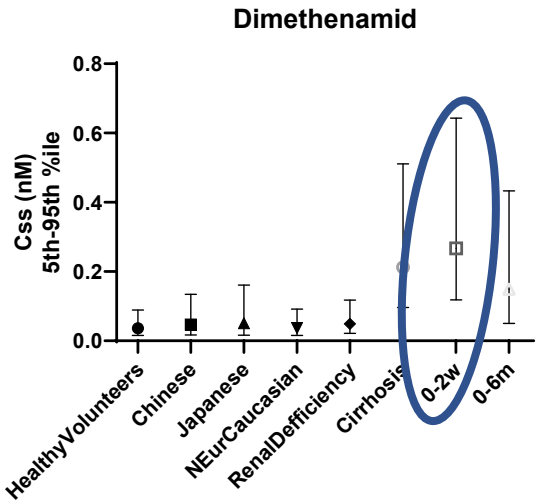
- Enzyme-specific clearance rates generated for 6 chemicals across 6 isozymes

Chemical	CYP1A2	CYP2C9	CYP2C19	CYP3A4	UGT1A1	UGT1A4
Ametryn	X		X			
Butylparaben	X	X	X		X	
Dimethenamid				X		
Fenbuconazole				X		
Fenhexamid		X	X		X	
Glyphosate						

- Subpopulation-specific plasma concentrations predicted

Patients with severe cirrhosis & 0-2 week olds generally the most sensitive groups





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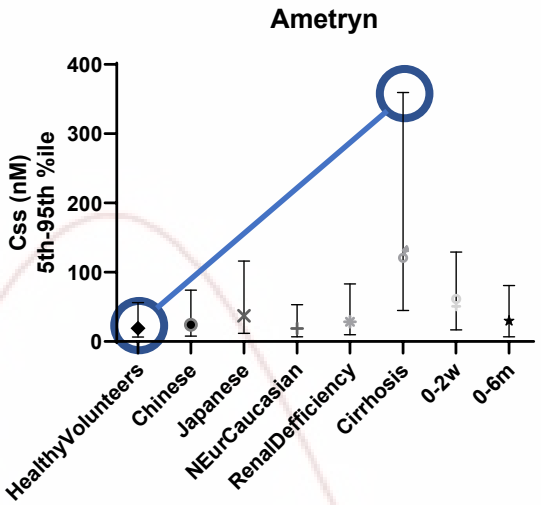
Impact & Future Directions

- Variability for sensitive populations exceeds the 3.2 default uncertainty factor for all chemicals thus far



- Data generation underway for 12 chemicals
- Exploring contributors to increased sensitivity

- Compare findings to exposure estimates to inform regulatory decision-making regarding uncertainty factors