

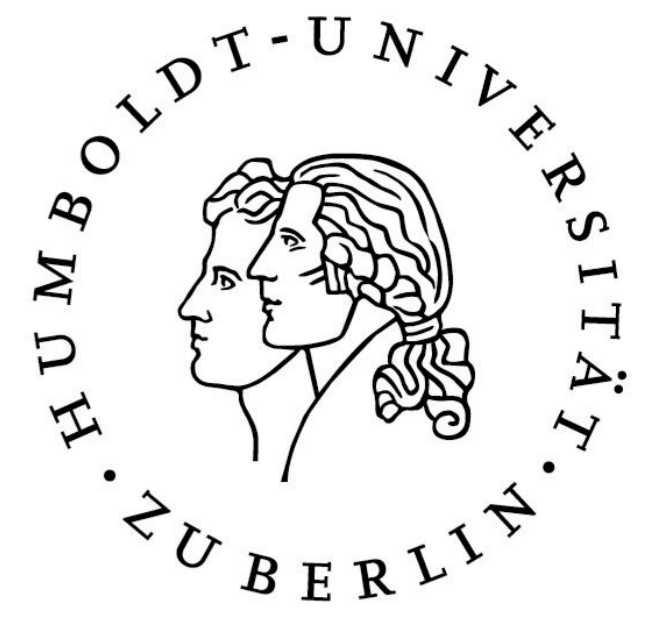
# Canagliflozin

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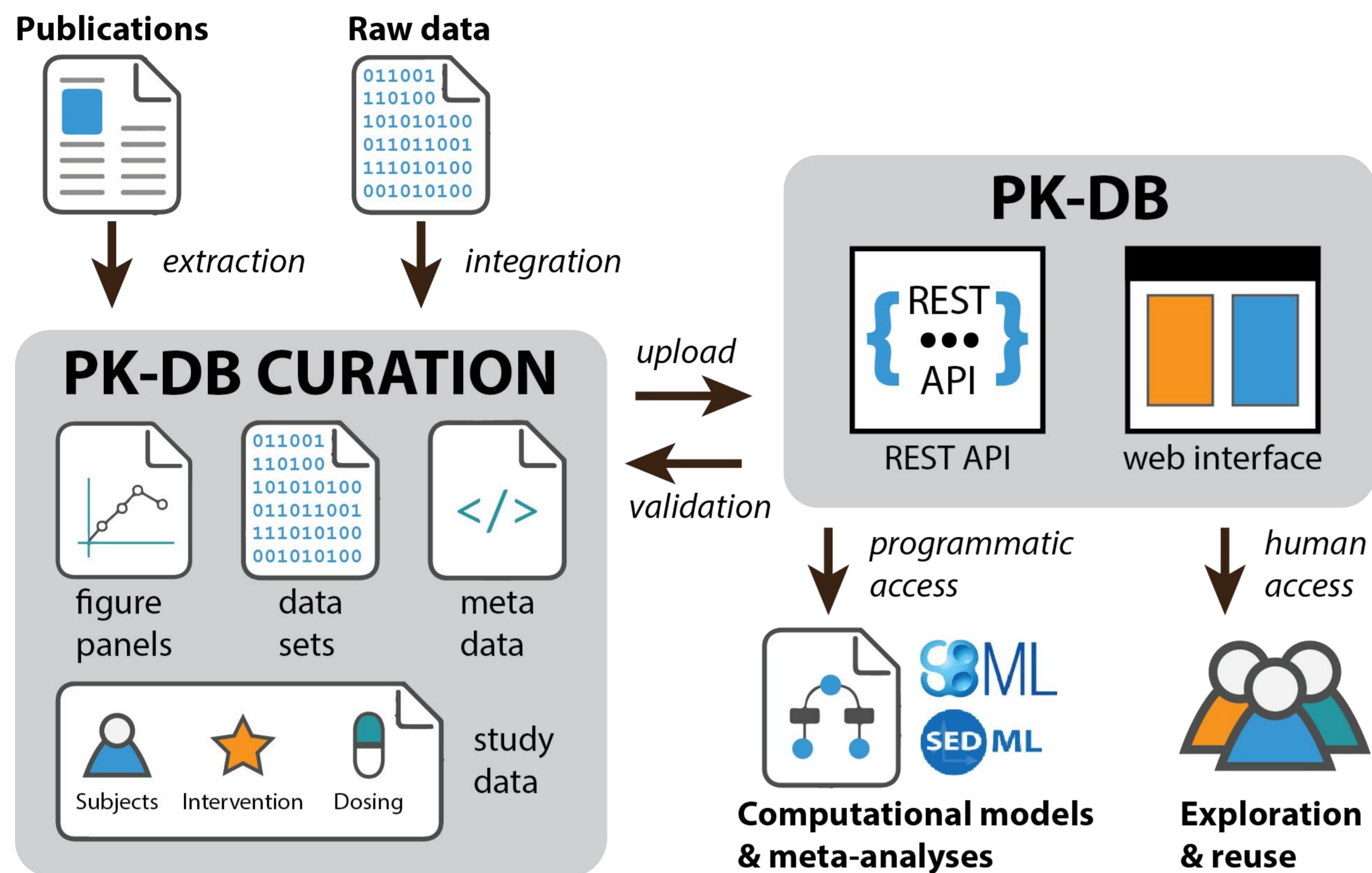
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## Background

In this project, we are developing a physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) model of the SGLT2 inhibitor canagliflozin. The aim is to improve our understanding of intra-individual variability in diabetes treatment with SGLT2 inhibitors, e.g. differences in hepatorenal function.



**Figure 1. PK-DB overview.** Schematic overview of the PK-DB data curation process. Figure panels, datasets, metadata and study information on subjects, interventions and dosing are curated from the publications. The uploaded study information can be accessed either programmatically via the REST API or via the web front-end.

Citation key	Title
Aharon-Hananel2020	An evaluation of the efficacy and safety of Tofogliflozin for th...
Alam2020	Quantitative determination of canagliflozin in human plasma s...
Algeelani2018	Inhibitory effects of sulfonyleureas and non-steroidal anti-inflam...
Ali2022	Cytochrome P450 3A4-mediated pharmacokinetic interaction ...
Alshehri2024	Repurposing the inhibitors of MMP-9 and SGLT-2 against ubiquitin sp...
Badragheh2018	Silica-coated magnetic iron oxide functionalized with hydrophobi...
Baira2018	Characterization of forced degradation products of canagliflozin...
Bhatia2014	Canagliflozin-current status in the treatment of type 2 diabete...
Boyle2014	A safety evaluation of canagliflozin : a first-in-class treatment for...
Ceriello2019	The Unique Pharmacological and Pharmacokinetic Profile of Te...
Chen2015	Pharmacokinetics, Pharmacodynamics, and Safety of Singl...
Chu2019	The SGLT2 Inhibitor Empagliflozin Might Be a New Approach f...
Cowart2024	A Review of the Safety and Efficacy of Bexagliflozin for the Ma...
Cui2022	Pharmacokinetic Interactions between Canagliflozin and Sor...
Dalama2016	[Glucose renal excretion as diabetes treatment: From an old diag...
Davidson2014	Sodium glucose co-transporter 2 inhibitors and their mechanis...
Deeks2017	Canagliflozin: A Review in Type 2 Diabetes.
Devineni2012	Canagliflozin improves glycaemic control over 28 days in...
Devineni2013	Pharmacokinetics and pharmacodynamics of canagliflozi...
Devineni2014	Effects of hydrochlorothiazide on the pharmacokinetics,...
Devineni2015	Effect of canagliflozin on the pharmacokinetics of glyburid...
Devineni2015a	Single- and multiple-dose pharmacokinetics and pharma...
Devineni2015b	Absolute oral bioavailability and pharmacokinetics of ca...

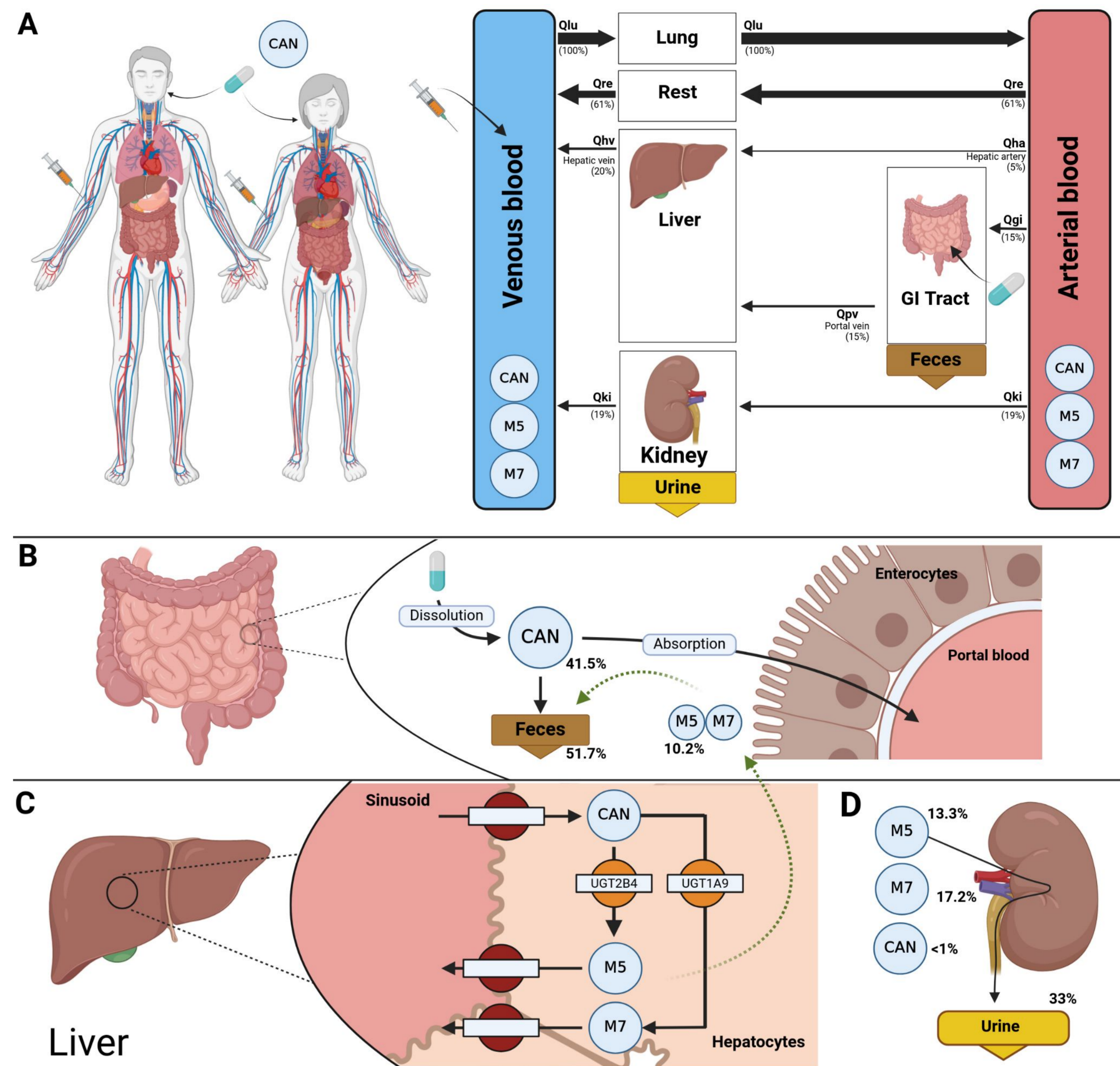
**Figure 2. Canagliflozin literature search.** A systematic literature search was performed in PubMed and PKPDAI for publications related to pharmacokinetics AND canagliflozin. All publications were manually evaluated, tagged according to the information found in the article, and sorted by priority for curation in PK-DB.

## Results

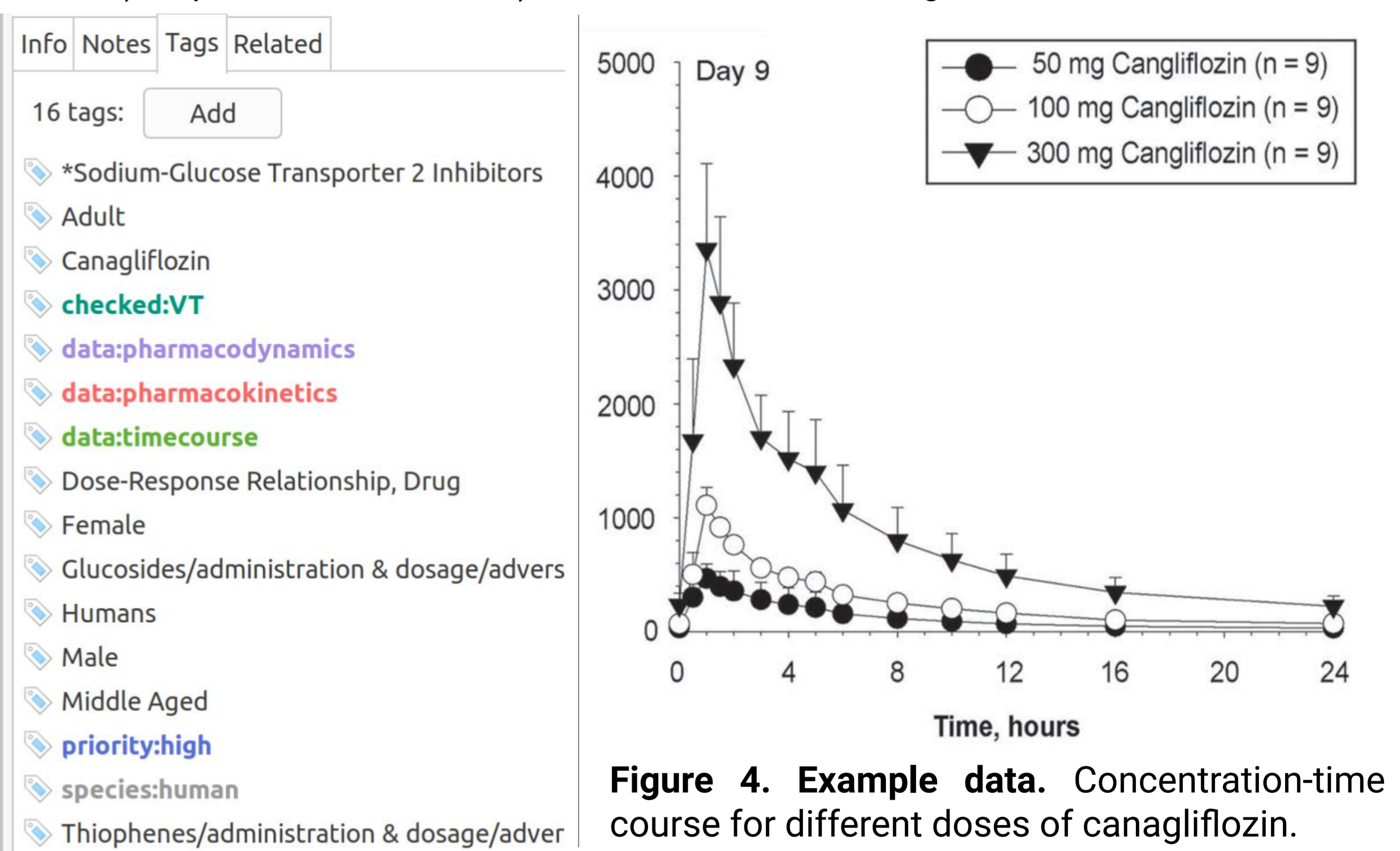
Zotero was used to review over 100 articles and extract relevant information. Important tags were assigned with colors (see Figure 2) and studies were prioritized for curation in PK-DB (see Figure 1). Studies were excluded if they involved non-human species, children, or if neither pharmacokinetic or pharmacodynamic data were available for canagliflozin. Examples of pharmacokinetic data of interest are shown in Figure 4.

## Funding

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**Figure 3. Overview of pharmacokinetics model of canagliflozin.** A) whole-body circulation of canagliflozin and metabolites M5 and M7. B) Intestinal absorption and enterohepatic circulation of metabolites. C) Hepatic metabolism. D) Renal excretion of canagliflozin and metabolites.



**Figure 4. Example data.** Concentration-time course for different doses of canagliflozin.

## Next steps

- Digitization of datasets for computational modeling
- Develop a physiologically based PBPK/PD model of canagliflozin
  - ordinary differential equations (ODE) model in SBML
- Model simulations & analysis

## Humboldt Internship Program (HIP) experience

During the internship, I had the unique opportunity to immerse myself in the world of scientific research in an international environment. My experience included both individual and team work, which allowed me to deepen my knowledge and skills in the field of biology. In addition, I had the opportunity to improve my social skills and make connections with students from all over the world. Overall, participating in the internship has already had a huge positive impact on my scientific career development, and I still have a lot to learn and experience in the next two months.

## References

- [1] PK-DB: pharmacokinetics database for individualized and stratified computational modeling. Grzegorzewski et al., Nucleic Acids Res. 2021, [10.1093/nar/gkaa990](https://doi.org/10.1093/nar/gkaa990).