Posterior parameter sensitivity analysis

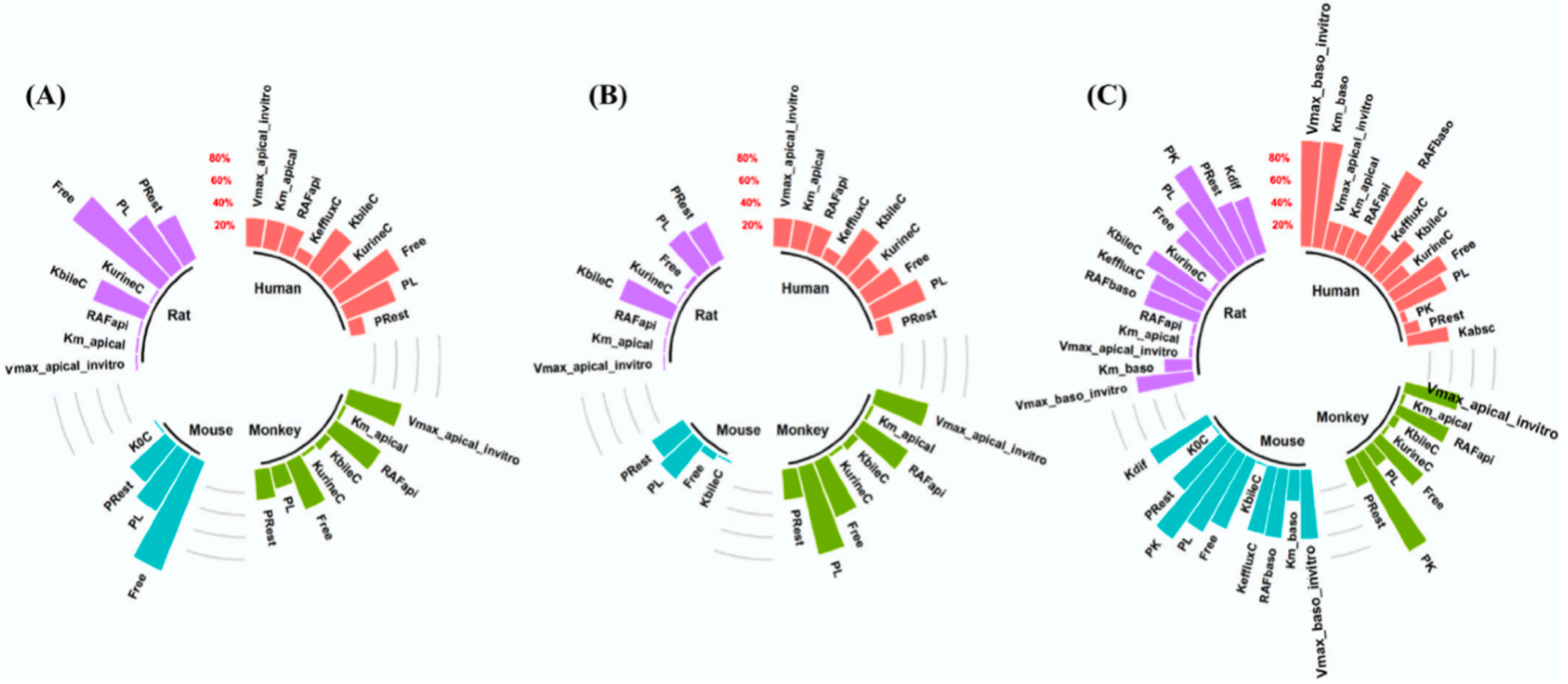

Fig. 6. Normalized sensitivity coefficients (NSCs) of posterior parameters using AUCs for concentrations of PFOS in (A) plasma, (B) liver, and (C) kidney in the mouse (single oral dose to 1 mg/kg/day), rat (daily dosing to 1 mg/kg/day for 98 days), monkey (daily dosing to 0.75 mg/kg/day for 182 days) and human (daily dosing to 4.5 ng/kg/day for 25 years). Only parameters with at least one absolute value of NSC > 1% are shown on the plots. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Predicting human equivalent dose

Compared species : rats and monkeys

- Find the posterior distribution of parameters and validate models via model prediction
- Use the validated models to predict response (plasma & liver) under no-observed-adverse-effect-level (NOAEL) doses of PFOS
  - rats : 0.34 mg/kg/day
  - monkeys : 0.15 mg/kg/day
- Calculate (plasma & liver) AUC at NOEAL exposure levels
  - rats [14 weeks] & humans [25 years]
  - monkeys [26 weeks] & humans [25 years]

$$\mathrm{HED} = \frac{\mathrm{AUC}_{\mathrm{species}}/\mathrm{duration}_{\mathrm{species}}}{\mathrm{AUC}_{\mathrm{human}}/\mathrm{duration}_{\mathrm{human}}} \cdot \mathrm{NOAEL}_{\mathrm{species}}$$