Supporting Information

Title: Structure-Dependent Hematological Effects of Per- and Polyfluoroalkyl Substances on Activation of Plasma Kallikrein−Kinin System Cascade

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Number of tables: 1

Summary of supporting information

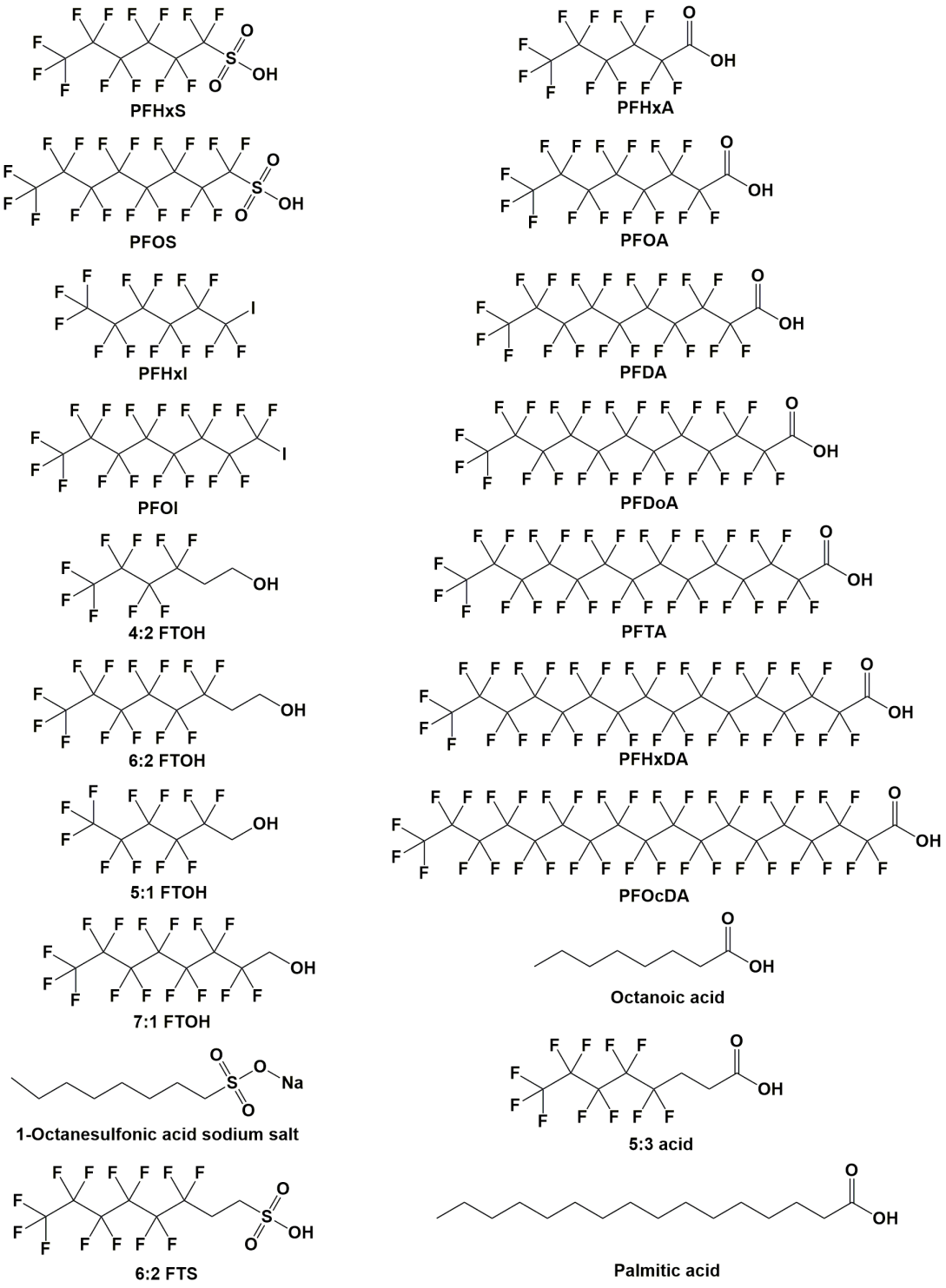

Fig. S1. Structures of PFASs and the related aliphatic compounds in this study.

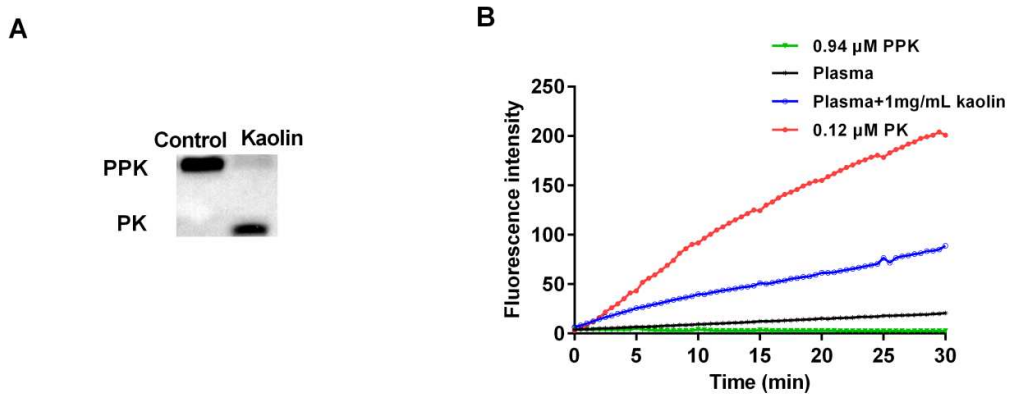

Fig. S2. Characterization of ex vivo PPK activation in mouse plasma. (a) Western blot for PPK cleavage in mouse plasma upon the stimulation of kaolin, a typical KKS activator. The PPK (~75 kDa) was abundant in the control plasma, while Kaolin treatment (1 mg/mL) caused the striking weakening of PPK band and the significant enhancement of PK band (~52 kDa), showing ex vivo PPK cleavage and KKS activation. **(b)** Kallikrein-like activity assay. The addition of Kaolin obviously increased kallikrein-like activity in plasma due to the induction of KKS activation.

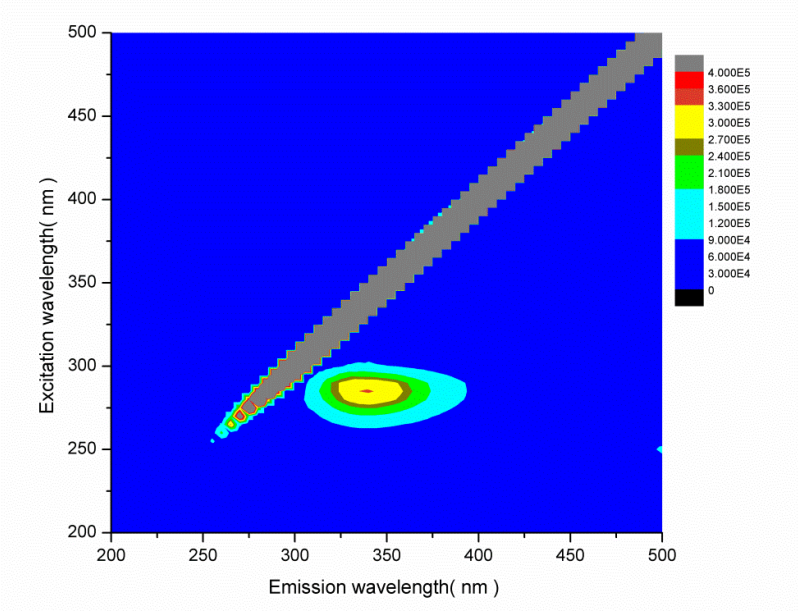

Fig. S3. The fluorescent characteristics of FXII. The monitoring of λ_{em} in the range of 300-450 nm showed the maximum value was 350 nm for FXII (λ_{ex} 280 nm).

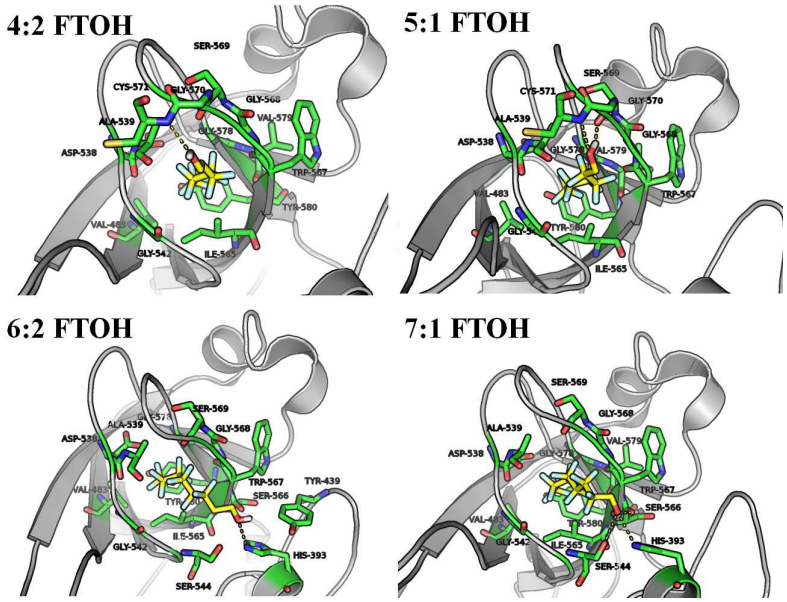

Fig. S4. The binding modes of FTOHs to FXII.

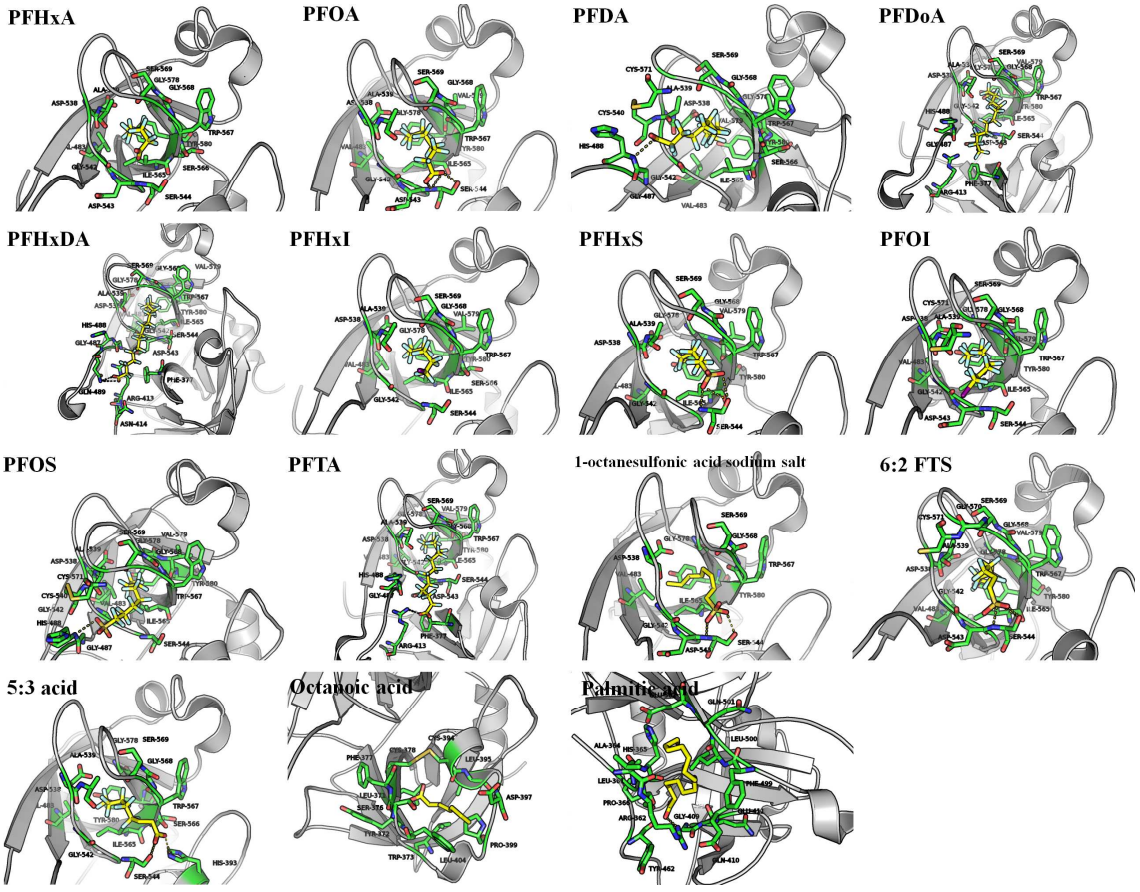

Fig. S5. The binding modes of PFASs and the related long-chain aliphatic compounds to FXII.

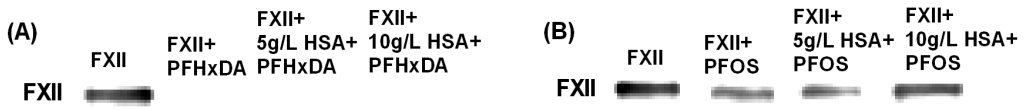

Fig. S6. Effects of HSA on PFAS-induced FXII activation. (A) 100 μM PFHxDA. **(B)** 5 mM PFOS. The level of FXII was 0.58 μM, and the concentrations of HSA were controlled at 5 and 10 g/L, respectively. The incubation lasted for 2 h.

Table S1. The calculated docking scores for the binding interaction energies between FXII and PFASs or the related long-chain aliphatic compounds tested in this study.

Structural factor		Compound	CAS	Docking score
Carbon chain length	Terminated with -COOH	PFOcDA	16517-11-6	**-10.04**
		PFHxDA	67905-19-5	**-9.69**
		PFTA	376-06-7	**-9.08**
		PFDoA	307-55-1	**-8.63**
		PFDA	335-76-2	**-8.23**
		PFOA	335-67-1	**-8.02**
		PFHxA	307-24-4	**-7.08**
	Terminated with $-SO_3H$	PFOS	2795-39-3	**-8.22**
		PFHxS	3871-99-6	**-7.69**
Terminal group	C6	PFHxS	3871-99-6	**-7.69**
		PFHxA	307-24-4	**-7.08**
		5:1 FTOH	423-46-1	**-6.88**
		4:2 FTOH	2043-47-2	**-6.45**
		PFHxI	355-43-1	**-7.3**

	C8	PFOS	2795-39-3	**-8.22**
		PFOA	335-67-1	**-8.02**
		7:1 FTOH	307-30-2	**-7.62**
		6:2 FTOH	647-42-7	**-7.29**
		PFOI	507-63-1	**-7.62**
Fluorine atom substitution degree	C8 terminated with $-SO_3H$	PFOS	2795-39-3	**-8.22**
		6:2 FTS	27619-97-2	**-7.59**
		1-octanesulfonic acid sodium salt	5324-84-5	**-4.77**
	C8 terminated with -COOH	PFOA	335-67-1	**-8.02**
		5:3 acid	914637-49-3	**-7.06**
		octanoic acid	124-07-2	**-4.86**
	C16 terminated with -COOH	PFHxDA	67905-19-5	**-9.69**
		palmitic acid	57-10-3	**-5.14**

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