INTRODUCTION

no ous sna s an t r v no s av nst bot ar an

FIGURE 1 | Duvernoy's venom gland and enlarged maxillary teeth of rear-fanged snakes. (A) *Spilotes sulfureus* **Duvernoy's venom gland** *in situ*. **Note that no muscles are directly associated with the gland—venom secretion is realized via compression of the gland between the skin and the contracting jaw adductor muscles. (B) Duvernoy's venom gland and supralabial gland of** *S. sulfureus*. **(C) Left maxilla (ventro-lateral view) of** *S. sulfureus* **showing three serially enlarged rear teeth. Bar = 5 mm. (D) SEg**

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FIGURE 2 | Reduced SDS-PAGE protein profiles for various rear-fanged snake venoms. Rear-fanged snakes tend to have either three-finger toxin-dominated venoms (A) or venoms rich in metalloproteinases (B)

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non tox n n s as v no prot ns an a to on oun n vo ut onary ana ys s- Expr ss on o n s b on n to v no tox ns s r n v no an t ssu s n o par son to ot r or an t ssu s an xa n n t s xpr ss on pro s as b n

TABLE 1 | Toxicity of venoms and purified toxins toward lizards and mice.

	LD_{50}–Lizards (Hemidactylus frenatus)	LD_{50}–Mice (Mus musculus)
CRUDE VENOM		
Naja kaouthia	1.02 μg/g i.p.	0.6 μg/g i.p.
Boiga irregularis	2.5 μg/g i.p.	31 μg/g i.p.
Spilotes sulphureus	1.01 μg/g i.p.	2.56 μg/g i.p.
PURIFIED TOXINS FROM VENOMS		
α-cobratoxin—*Naja kaouthia*	<0.1 μg/g i.p.	<0.1 μg/g i.v.
Irditoxin—*Boiga irregularis*	0.55 μg/g i.p.	>25 μg/g i.p.
Sulditoxin—*Spilotes sulphureus*	0.22 μg/g i.p.	>5 μg/g i.p.
Sulmotoxin 1—*Spilotes sulphureus*	>5 μg/g i.p.	4 μg/g i.p.
Sulmotoxin 2—*Spilotes sulphureus*	>5 μg/g i.p.	>5 μg/g i.p.

i.p., intraperitoneal; i.v., intravenous.
Lethal dose (LD_{50}) values for B. irregularis venom are from Mackessy et al. (2006), S. sulphureus venom are from Modahl et al. (2018b), and N. kaouthia venom are from Modahl et al. (2016). Purified α-cobratoxin values are from Modahl et al. (2016) (lizard) and Karlsson (1973) (mice), irditoxin values are from Pawlak et al. (2009), and purified toxins values from S. sulphureus are from Modahl et al. (2018b).

LD xp r nts a ssy - *Phi dryas patagoniensis* v no was t st on p ons *Co ba ia do estica,* u n a p s *Cavia porce s,* rabb ts *Orycto gus cunicu s,* an ro s *Leptodacty s*

o on y us stru to ass b tox n n s b aus o
t u t tu o s ar so or s an xpr ss on v s o

FIGURE 3 | Taxon-specific three-finger toxin (3FTx) sequences (A) and structures (B). (A) Characterized lizard specific 3FTxs are shown in green, and su

vo ut on n r ar an sna v no s an prov y ns ts nto v no vo ut on an pr atory strat s as t s sna s vary r at y n pr atory b av or an typ s o pr y onsu - n atyp a pr y t s ar ta n v no prot ns w t un qu a t v t s ay b s ov r - s as b n t as or s v ra FF sp s su as sna s t at onsu ot r sna s- K n Cobra *Ophiophagus hannah* s a sp s t at onsu s ot r sna s an was oun to av a tox n ro a n w v no prot n sup r a y o ann n ts v no un ta - - Lon an Cora na *Calliophis bivirgatus* a so a sna at n sna was oun to av a F x w t unusua a t v ty towar so u on ann s Yan ta - - na s o t nus *Bungarus* w a so o on y on ot r sna s x b t un qu F x o o r o p x s κ bun arotox ns: D wan ta - - ar an sna s av v n or tary sp a sts n u n sp s t at on s orp ons sp rs or nt p s an so t s xp t t at nov tox ns r an to b s ov r n v no s o t s v rs roup o o ubro sna s- r or t s y t at v no s ro F sp s pot nt a y av any n w an urr nt y un s ov r pot nt tox ns- Exp r nta stu s av oun t at on y about a o t tota v no xp n by t F *B irregularis* s v r nto t v s ra o pr y an t ot r a r ans b nt s n Hay s ta - - But v n w t t s ow r y s v r nto pr y t ssu ts ar st obs rv as pr y t at s r ov w t out b n onsu by t sna ay b o s u s an v ntua y a t r any nut s or s v ra ours Hay s ta - - In o b nat on w t a ss rap v no v ry syst t s sna s a so n ra y av ss o p x v no a ssy b oto t a - r su t n n v no tox ns t at ar opt or sp typ s o pr y- no s ro ost sp s o F ar un ara t r an b aus o stor b as s ost LD wor ut s o st urn o s u to ava ab ty o n t un or ty an pr su os r app ab ty to u ans- How v r by x u n ot r o s su as ar s ot r v rt brat s an nv rt brat s on an ov r oo t b o o a pot n y o sp a v no prot ns t at ay av b n s t or tox ts on non a an pr y - ar s ta - y a t rs ta - -

Digestion

ta oprot nas s n ratt sna v no s av b n su st to a tat nt st on o pr y at subopt a t p ratur s or w n ar pr y ar onsu a ssy a: ow v r s v ra stu s av n at t at nv no at on o s not n r as st y a y Cu : C u ta - - In t as o any ratt sna sp s t xt nt o a t v ty n a v no s n at v y orr at w t ov ra v no tox ty a ssy a - s as to ratt sna v no s b n ara t r as typ I o nat v no s t at ar ss tox or typ II v no t at s or tox but w t ow ta oprot nas a t v ty: a ssy a- A s ar oto y s oun n any F v no s w r a v no s t r o nat by tox F xs or n y at s G v rn t a - - For t F v no s t at ar av y o nat by s t s v no o pon nts y a so a n pr y pr st on as s ar br no no yt a t v ty s obs rv or s ro bot ratt sna s an F sp s o a t a - a- tu y n F v no s an r v a para s to tr n s s n n FF v no s p as n t portant o sp v no prot ns n a tat n pr y an n n v rs sp s o v no ous sna s r ar ss o t v no v ry syst -

FUTURE RESEARCH

A van nts an nt rat ons o r s ar t no o s now a ow u or ta approa s to ara t r un nown v no s an n v ua tox ns- rans r pto s ass b ro v no an s prov usto atabas s to b par w t prot o s an a t poss b to nt y prot ns n a v no v n w n t y ar urr nt y ss n ro pub atabas s o a ta - - For t r nty ara t r su tox n w t out t sp s sp G trans r pto nt rpr tat on o t sp tra o t tryps n st tox n by s ar n a a nst pub o a n atabas s not r su t n nt at on o t s so at tox n- By n u n t G v no an trans r pto t nt at on o t xa t trans r pt an t us t u a no a s qu n was r a y a v o a ta - b r v ous y a s ar s tuat on pro u n at v r su ts: ro t ana ys s o F *Rha phiophis oxyrhynchus* v no a n urotox n was so at an part a y ara t r but t s ow no s ar t s to any tox ns n pub atabas s at t at t an t xa t v no prot n ass at on ou not b t r n Lu s n ta - - n qu or unusua tox n s qu n s st ay not b pr s nt n pub atabas s an n sp s sp v no an trans r pto atabas s ar r t a or nt at on Ca pos ta - : o a ta - b - w r t no o s av a ow or o at ons to var ous ara t r at on approa s- For v no an trans r pto ass b s v no prot n nt t s ar usua y bas on nown y wor s ar s or tox ns- or r nt y s v ra a n arn n pro ra s av b n v op to nt y un nown tox ns ro ar trans r pto atas ts Ga sa ta - : a ran r ta - - A t ona y s qu n n ot r sna t ssu s b s s v no an s as prov ns t nto ow n xpr ss on an p n t nt at on o tru tox ns w at an s s r su t n tox n xpr ss on n t v no an n o par son to ot r t ssu s an w at n o o o s ar pr s nt n ot r t ssu s Har r av s ta - : Junqu ra A v o ta - : y s as o ta - - G no s o F ar a so us u to nt y tox n n up at on v nts rry ta - - y p to prov support to approa s to nt y w r tox n n s or nat an s t on pr ssur s t y xpr n -

B aus r ar an v no ous sna s n o pass su a ar v rs ty o o ubro sna s v no vo ut on an b stu on a broa r vo ut onary s a a r ss n su qu st ons as t t o p y o ny on v no vo ut on or tary sp a at on- r s an xtr ran o tox ty o F v no s to u ans w t so sp s b n t r at n an ot rs b n ar ss s ra nt o tox ty an b us or xp orat ons nto v no n t r s o t b o o a ro s o n v ua v no prot ns su as ow tox ty an pr y sp ty an y op- no s ro r ar an sna s s ow any para s to t os o FF but on ar a t at as y t to b xp or s t v o v no var at on w t n a s n F sp s- v no o *B irregularis* as b n oun to x b t onto n t var at on r at to t an v no s ro r nt popu at ons In on s a vs- Gua s ow onstrab y r nt tox n o pos t ons a ssy t a- a t a- a -Conv rs y n v ua s ro t sa popu at ons o *B portoricensis* an *A prasina* s ow v ry tt v no var at on o a t a- a but popu at on v var at on n v no o pos t on s urr nt y un nown or F - ar at on n r ar an sna v no s s rv s or att nt on as t an p to un ov r t an s s b n o on y obs rv v no var at on w as b n an ar a o ontrov rsy- tu s ar a so st a n at t v o posttrans at ona o at ons o v no prot ns or ost v no ous sna s an ow t s ontr but s to ov ra v no v rs ty-

Anot r n t ar a o r s ar s t nt ra t v or syn r st pot nt a o tox ns- B aus stu y n pur tox ns usua y r qu r s a r u t on st approa w stu s av att pt to va uat nt ra t ons b tw n tox ns- D r tox ns su as su tox n an r tox n ons st o two ss ar F xs but t portan o r asso at ons to sp

Casto -A- Kon n A- -J- Ha K- - Car D-C- D- -Fu ta - K- t a - - Bur s pyt on no r v a s t o u ar bas s or xtr a aptat on n sna s- *Proc Nat Acad ci A* , - o , - , pnas-

H - E- an a ssy - - - no y s ro s v ra sp s o
o ubr sna s an r nt a ts o ta n - *oxicon* -

on C- L- an a ssy - - - A sop nas a n w III ta oprot nas w t a p a br no no yt an orr a a t v ty ro t v no o t r ar an u rto an a r *A ophis portoricensis* rp nt s D psa a - *Biochi ie* - o - b o

Ya a a Y- Ko H- u ya a Y- otoyos K- a a - H s nu a - t a - - C on n an ara t r at on o nov sna v no prot ns t at b o s oot us ontra t on- *Eur J Bioche* - o - -x

Yan D- C- D u s J- - Das vs y D- Dobson J- Ja son - - - Brust A- t a - - na w t t s orp ons st n nov t r n r tox n