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Dear Editor,

Please consider our manuscript entitled “Snake venom potency and volume are driven by metabolism, dimensionality and prey characteristics” for publication as a research article in *Proceedings of the National Academy of Sciences.*

People have long been fascinated by venomous snakes because of their ability to cause death and harm. Venom is also of interest to medical researchers due to both human physiological responses and potential as a source for new drugs. Despite our interests, little is known about the evolutionary drivers of snake venom despite the potential to explain vast differences in toxicity, (e.g. inland taipan can kill 100,000’s of prey while the marbled sea snake holds minuscule amounts of weak venom). However, a major barrier allowing a consistent comparative approach of venom is the difficulty of comparing potencies where measures are based on very different lab (model) species many of which are unrelated to the snakes natural prey. We overcome this by taking a novel approach by accounting for the evolutionary distance between the model species and the types of species naturally in their diet.

Using this approach, we find that potency is greater in model species closely related to natural prey – indicating that venom is adapted to incapacitate common prey. Examining patterns in venom volume, we also find that volume varies in a manner consistent with size-related changes in metabolic rate, rather than that predicted by the scaling of snake prey body, increased reduces the amount of venom.

These findings have novel implications for our understanding of not only venom evolution and ecology? in snakes but, may have implications for venom evolution in other groups and predator trait evolution in general. Our results resolve a long standing debate within the field of venom evolution but also provide novel findings regarding the effects on venom of body size and habitat dimensionality..

We think our paper will make an excellent fit for PNAS due to its general appeal to both the public and research fields ranging from the biomolecular sciences to ecology and evolution. Our paper also reflects similar papers on venom evolution and macroecological patterns published in PNAS ([5](#_ENREF_5), [12](#_ENREF_12)).

We look forward to hearing from you in due course

Kevin Healy, on behalf of my co-authors

The manuscript contains xxx words in the main text, and we estimate the paper will require 6 pages. None of the material has been published or is under consideration elsewhere.

**Suggested Referees**

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We could go for the metabolic people such as Jim Brown?