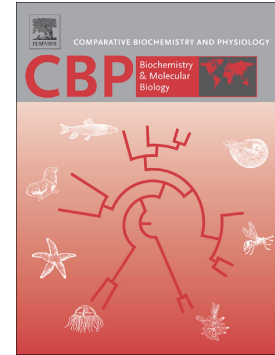


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Comparative Biochemistry and Physiology – Part B: Biochemistry & Molecular Biology

## **Snakes exhibit tissue-specific variation in cardiotonic steroid sensitivity of Na<sup>+</sup>/K<sup>+</sup>-ATPase**

**Shabnam Mohammadi<sup>1,2</sup>, Georg Petschenka<sup>3</sup>, Susannah S. French<sup>1,2</sup>, Akira Mori<sup>4</sup>, Alan H. Savitzky<sup>1,2</sup>**

<sup>1</sup>Department of Biology, Utah State University, Logan, UT 84322, USA

<sup>2</sup>The Ecology Center, Utah State University, Logan, UT 84322, USA

<sup>3</sup>Institut für Insektenbiotechnologie, Justus-Liebig-Universität Giessen, Heinrich-Buff-Ring 26-32, 35392 Giessen, Germany

<sup>4</sup>Department of Zoology, Kyoto University, Sakyo, Kyoto 606-8502, Japan

**Author for correspondence:**

Shab Mohammadi e-mail: shab.mohammadi@gmail.com

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### **ABSTRACT**

Toads are among several groups of organisms chemically defended with lethal concentrations of cardiotonic steroids. As a result, most predators that prey on amphibians avoid toads. However, several species of snakes have gained resistance-conferring mutations of Na<sup>+</sup>/K<sup>+</sup>-ATPase, the molecular target of cardiotonic steroids, and can feed on toads readily. Despite recent advances in our understanding of this adaptation at the genetic level, we have lacked functional evidence for how mutations of Na<sup>+</sup>/K<sup>+</sup>-ATPase account for cardiotonic steroid resistance in snake tissues. To address this issue, it is necessary to determine how the Na<sup>+</sup>/K<sup>+</sup>-ATPases of snakes react to the toxins. Some tissues might have Na<sup>+</sup>/K<sup>+</sup>-ATPases that are more susceptible than others and can thus provide clues about how the toxins influence organismal function. Here we provide a mechanistic link between observed Na<sup>+</sup>/K<sup>+</sup>-ATPase substitutions and observed resistance

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