Animals living in changing environments experience variations in resource availability, climate conditions and threat of predators and pathogens. Thus, they must allocate endogenous resources among competing physiological processes to maintain homeostasis and survive. Immune defense is an important determinant of animal fitness, but is costly in terms of inevitable trade-offs with other energy-demanding processes. Therefore, if the immune system is to be bolstered, other physiological functions competing for the same energy resources must be traded-off. Conversely, allocation of energy in other physiological systems, such as reproduction or chemical defense, is likely to impair immune responses and thus makes animals more vulnerable to parasites and pathogen attacks. Chemical defense is widespread in the animal kingdom and animals use toxic substances for prey capture, competition and defense against predators and pathogens. Most animal poisons consists of many compounds with varied activities. Some of them can contain up to several hundred toxins. Production of such highly toxic secretions can be metabolically costly and thus may require a high energy expenditure. Toxin synthesis and abundance depend on energy resources. Therefore, animals in good condition may restore their toxins faster than those in poor condition. If large amounts of energy are spent on synthesis of new toxins, poison production may negatively affect other physiological processes, e.g. immune activity. Here we propose to test the hypothesis that ability to maintain chemical defense is a resultant of a trade-off between poison production and somatic maintenance. Toads are good candidates to study the link between toxicity and physiology, because they produce and store potent toxins in their skin glands. Poison of a single toad can contain over 100 toxins, many of which (e.g. bufadienolides) are derived from lipids and thus may be energetically expensive to produce. Process of poison regeneration in toads appears to be slow. Moreover, it has been shown that poison depletion reduces the growth rate of cane toads and lowers their dispersal abilities. The aim of our project is to investigate the costs of poison regeneration and determine the impact of toxin replacement on energy expenditure and mechanisms of immune defense in toads as model animals. We hypothesize that poison replenishment affects the energy budget of toads. Therefore, poison depletion should lead to the increase of toad metabolic rate. Then, if poison production is energetically expensive, we expect that poison replenishment leads to the disturbance of homeostasis inducing stress response, and thus results in elevated level of corticosterone, stress hormone, in blood and neutrophils to lymphocytes [N:L] ratio. In turn, stress induced by poison depletion may reduce immune function and lead to changes in organ physiology and morphology. Namely, to replenish poison toads require a large and active liver, in which lipid precursors for bufadienolides are synthesized, and animals in better condition are likely to regenerate poison faster and it should be of better quality than in animals with limited food resources. Finally, we hypothesize that there is a trade-off between poison replenishment and immune response of toads. We expect that energy resources required for poison replenishment diminish the pool of resources necessary to maintain immunological response. Because poison production and immune function compete for the same energy resources, we predict that immune challenge prioritizes immune defense resulting in lower investment in poison replenishment. With this project, we will be able to assess the metabolic costs of toxin production and effects of poison replenishment on energy partitioning in poisonous animals. This will extend our knowledge on the role of toxins in animal physiology and provide important insights into trade-offs in energy allocation. The results will be of great importance for animal conservation, particularly amphibians. Pathogen infections are crucial agents causing amphibian extinctions. Toads with weakened immunological responses may be more vulnerable to microbial infections. Therefore, evaluating the costs of poison replenishment and understanding a trade-off between poison production, stress response and somatic maintenance will allow us to understand how poisonous vertebrates cope with the predation risk and environmental conditions in nature. To the best of our knowledge, our research will be the first describing the relationship between poison production and immunity in amphibians as model animals.