Host-defense peptides and proteins (HDPs) are considered a vital part of the innate immune system, protecting surfaces and tissues against a broad diversity of pathogenic microorganisms. Whereas some classes of vertebrate HDPs (vHDPs) are shared by lineages as diverse as teleost fishes and placental mammals, amphibian skin secretions contain unique HDPs (aHDPs) that represent a unique class of cytolytic peptides. I combined transcriptomic, genomic and phylogenetic analyses with functional tests to provide new insights in the diversity and evolution of the amphibian HDP arsenal.

First, through a transcriptome study of the pipid frog *Hymenochirus boettgeri*, several peptide and protein families were identified as candidate aHDPs and/or sex pheromones. Two new protein families were described, with domains unlike those in any other species. More detailed analyses revealed that this frog species secretes at least 15 aHDPs with surprisingly low structural variation. This pattern is in remarkable contrast to the broad aHDP diversity observed in other frogs, including closely related pipid genera, and may be explained by purifying selection, recent duplications or concerted gene evolution.

Besides newly evolved aHDPs, many amphibians may have also retained evolutionary ancient vHDPs. Using genome screening, I show that four of the major vHDP families are represented by a similar number of genes in the genome of the pipid frog *Silurana tropicalis* as in amniote genomes, indicating that amphibian-specific aHDPs did not make these ancient vHDPs redundant as their genes have been coexisting in the pipid genome for over 100 million years. However, the vHDP family of defensins, which has undergone considerable duplication in most amniotes, is only represented by few genes in amphibians. Additionally, I show that the defensin genes of *S. tropicalis* belong to two different gene lineages that diverged early in tetrapod evolution. A similar phylogenomic study lead to the discovery in amphibians of an orthologue of S100A7, an HDP that was only known from mammals. Functional assays indicate that the cytolytic activity in this HDP evolved early in tetrapod evolution.