A longstanding interest of our laboratory is to study cysteine-rich peptides (CRPs) from medicinal plants as an inspiration to design orally-active compounds. Plants produce CRPs as part of their host-defense mechanism against microbes and insects. Most CRPs contain 15 to 25% of cysteine per molecule and are characterized by their cystine scaffold [1-5]. CRPs can display both hydrophilic and hydrophobic surface patches due to the cystine dense core which causes hydrophobic side chains to flip outwards, resulting in a unique “inside-out” feature. As hydrophobicity is a major driving force for cell penetration [6], we hypothesized that CRPs penetrate cells and bind to intracellular targets to exert their biological effects. Here, we report the discovery of hyperstable and cell-penetrating CRPs, roseltide rT1 and rT7, from *Hibiscus sabdariffa* of the Malvaceae family.

**CONCLUSIONS**

- Roseltide rT1 is a mitochondria-targeting peptide
- Roseltide rT7 is cell-penetrating and a proteasome-inhibiting peptide
- Hyperstable CRPs are cell-penetrating and targets intracellularly to elucidate their biological effects.

**REFERENCES**