Title- Applications of Novel Membrane Active Peptides

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Multiple biological applications attribute to membrane interacting property of membrane-active peptide (MAP). These peptides interact with the lipid membrane to either disrupt the membrane or cross the membrane without causing any damage. Among the membrane interacting peptides, cell-penetrating peptides cross the cellular membrane and deliver the cargo molecule to the cytosolic environment. Some cell-penetrating peptides have been shown to deliver the cargo molecules to a targeted location or specific organelle, and hence called organelle targeting peptides (OTP). Further, peptides causing alteration of the biological membrane leading to the death of microbes are termed antimicrobial peptides (AMP). Antimicrobial peptides are further classified according to their target pathogens, such as anti-bacterial peptides, anti-fungal peptides and anti-parasitic peptides.

In the present work, organelle targeting cell-penetrating peptides has been designed and screening of anti-parasitic peptides primarily related to *Leishmania donovani* has been carried out. We have shortlisted a chloroplast targeting cell-penetrating peptide (cTP) from the signal sequence of chloroplast targeting proteins. cTP enters the protoplast in less than five minutes and localizes in the chloroplast only. It also showed cargo delivery ability, as it could deliver DNase I protein to the chloroplast.

Also a domain of Vir D2 protein of *Agrobacterium tumefaciens* was employed and screened for its nuclear targeting and cargo-carrying property. It was also found that the importance of positive charge at peptide terminal strongly depends on the cargo attached.

Further, an inventory of membrane active peptides was screened for anti-leishmanial activity. India accounts for many patients suffering from the most lethal form of leishmaniasis, visceral leishmaniasis, proving fatal if left untreated. Drug resistance towards the drugs available for treatment and the absence of a vaccine and alternative drug therapies are significant concerns. Tachyplesin peptide derived from horseshoe crab showed anti-leishmanial activity without significant cytotoxicity at working concentration. The membrane dependent killing of the pathogen appeared to be a Tachyplesin killing mechanism. Thus, Tachyplesin emerged as a potent anti-leishmanial peptide.