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Delivery of lethal dsRNA in insect diets by branched amphiphilic peptide nano-capsules

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Branched Amphipathic Peptide Capsules (BAPCs) are biologically derived, bilayer delimited, nano-vesicles capable of being coated by or encapsulating a wide variety of solutes. The vesicles and their cargos are readily taken up by cells and become localized in the peri-nuclear region of cells. When BAPCs are mixed with DNA, the BAPCs act as cationic nucleation centers around which DNA winds. The BAPCs-DNA nanoparticles are capable of delivering plasmid DNA and RNAs *in vivo* and *in vitro* yielding high transfection rates and minimal cytotoxicity. In this study, we inhibited expression of two insect genes, BiP and Armet, through the ingestion of dsRNA complexed with BAPCs. The dsRNA-BAPCs complexes were added to the diets of two insect species from two Orders: *Acyrthosiphon pisum* and *Tribolium castaneum*. The gene transcripts tested (BiP and Armet) are part of the unfolded protein response (UPR) and suppressing their translation resulted in lethality. For *Acyrthosiphon pisum*, ingestion of <10 ng of BiP-dsRNA associated with BAPCs led to the premature death of the aphids ($t_{1/2}$=4 - 5 days) compared to ingestion of the same amounts of free BiP-dsRNA ($t_{1/2}$=11-12 days). *Tribolium* was effectively killed by ingestion (by larvae only) using a combination of BiP-dsRNA and Armet-dsRNA complexed with BAPCs (75% of the subjects, n=30) died as larvae or during eclosion (the emergence of adults from pupae). Feeding the two dsRNA alone resulted in fewer deaths (30% with n=30). These results show that complexation of dsRNA with BAPCs greatly enhances the oral delivery of dsRNA over dsRNA alone in the diet. This approach provides a simpler method of delivering dsRNA compared to microinjection for studying *in vivo* protein function and for developing novel strategies for pest management.

Biography

John M Tomich obtained his PhD in Chemistry from the University of Waterloo (Ontario, CANADA) and completed fellowships at the University of Delaware and Caltech. He is currently Professor of Biochemistry and Molecular Biophysics at Kansas State University. He has published over 15o journal articles, book chapters, published patents and books. He has severed on a number of NIH study sections and serves as an external advisor to several NIH program projects. His lab's interests have focused on utilizing Nature's rules for peptide self-assembly to design new structures with unique properties. We currently study patented bilayer delimited nano-capsules formed by the self-assembly of branched amphipathic peptides.

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