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New microRNA biotechnology to inhibit inflammation and regenerate bone

Current tools for the inhibition of microRNA (miR) function are limited to modified antisense oligonucleotides, sponges, and decoy RNA molecules and none have been used to understand miR function during development and they have very limited therapeutic applications. We report a novel plasmid-based miR inhibitor system (PMIS) that inhibits miR family members in cells and mice. The PMIS engineered optimal secondary structure, flanking sequences and specific antisense miR oligonucleotide sequence bind the miR in a stable complex to inhibit miR activity. In cells, one PMIS can effectively inhibit miR family members that share the same seed sequence. A complete family of miRs can be inhibited with a single plasmid. Different PMIS miR inhibitors can be linked together to knockdown multiple miRs expressed from different chromosomes. The PMIS shows no off-target effects or toxicity and is highly specific for miRs sharing identical seed sequences. Transgenic mice expressing PMIS-miRs reveal different developmental processes affected by miRs. Genome-wide analyses of PMIS transgenic mice and cells identified new miR regulated gene networks. We have identified miRs that control inflammation through the direct targeting of pro-inflammatory cytokines. We have developed a system to deliver the PMIS to regenerate bone, inhibit TMJ inflammation and osteoarthritis. Importantly, the non-toxic nature of the PMIS molecule makes it promising platform for the delivery of miR inhibiting effects that could have potential as a treatment of human diseases and genetic defects, something that has proven difficult for traditional oligonucleotide approaches to miR inhibition.

Biography

Brad A Amendt completed his PhD at the University of Iowa in 1994. He was an Assistant Professor at the University of Tulsa, Tulsa, OK, Professor and Associate Dean at the University of Texas A&M Health Science Center, Institute for Biosciences and Technology, Houston, TX. He is currently the Associate Dean for Research and Director of the Craniofacial Anomalies Research Center at the University of Iowa, Iowa City, IA. He has published more than 70 manuscripts, several books and book chapters and is the Founder and CSO of NaturemiRI, LLC. His team is developing clinical trials to test new biotechnology.

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