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Designer Biologics: BMP Chimeras and their clinical potential

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Discovery of new biologics presents new challenges and opportunities and revenues for biologics are rapidly growing in biopharmaceutical industry. We exploited our detailed structural knowledge of three-dimensional structures of BMPs, their receptors, and their antagonists to engineer synthetic BMP ligands. By use of a novel protein engineering strategy that we termed RASCH (Random Assembly of Segmental Chimera and Heteromers), we have set out to design a synthetic biologic (synbiologics®) for bone and cartilage therapy. In the case of bone fusion, we have used Activin and BMP-2, which are the members of TGF-beta superfamily, to create AB204 (Allendorph et al., 2011). AB204 is a synthetic 50:50 chimera of the two ligands, which indeed shows highly effective bone-forming capability. In the case of cartilage, we have used Activin and BMP-6 to create AB604, again a 50:50 chimera of the two. AB604 shows all the properties of super BMP6, surpassing the functional characteristics of natural BMP6. This approach promises to be a very powerful way to harness different biological functionalities of natural ligands to merge into one synthetic designer molecule such that it goes beyond what Mother Nature could provide a new means to meet various unmet clinical needs.

Biography

Senyon Teddy Choe, is a Professor of Biology and the Founding Director of Drug Discovery Collaboratory at UCSD. He pursued PhD in Biophysics and Medical Physics at Univ. California, Berkeley. He joined the Salk Institute in 1993 as the founding Faculty Member of the Institute's new Structural Biology Laboratory, and remained so through 2015. His research group has focused on understanding how cells talk to each other. An extension of these works explores designing synthetic biologics to modulate stem cells and sick cells directly. His major honors include election in 1999 to the Fellow of American Association for the Advancement of Science. He recently founded joint Center for Biosciences to translate discovery to medical applications to focus on protein engineering and developing new stem cell therapy. He currently leads Mogam Institute for Biomedical Research in Korea aiming for biologics discovery in the areas of infectious diseases and cancer.

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