My Journey in Translational Research: From Designing Integrin-Specific Drugs with Disintegrins to Developing Cell Therapies with Interleukin-2

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In our study, we focus on developing integrin-specific drugs for conditions such as diabetic retinopathy, cancer, and myocardial infarction, as well as on engineering interleukin-2 (IL-2) mutants for cancer treatment and the treatment of autoimmune diseases. Integrins are αβ heterodimers expressed on nearly all adhesive cells. They play crucial roles in various cellular processes and contribute to the initiation and progression of many prevalent diseases. Disintegrins are a group of RGD-containing proteins found in snake venoms, consisting of 47 to 84 amino acids and containing 4 to 7 disulfide bonds. These proteins bind to various integrin subtypes with high affinity. In our research, we successfully expressed rhodostomin (Rho), a 68-residue disintegrin with six disulfide bonds, in *Pichia pastoris*. We demonstrated that Rho can serve as a molecular scaffold for the design of integrin-specific antagonists. Our findings revealed that Rho mutants containing the AKGDWN and ARLDDL motifs can selectively inhibit the integrins αIIbβ3 and αvβ3, respectively. The 3D structures and backbone dynamics of these integrin-specific disintegrins were determined using NMR spectroscopy and X-ray crystallography. Additionally, cryo-electron microscopy was employed to ascertain the 3D structure of the integrin αvβ3-Rho complex. Based on animal disease models, we found that integrin-specific disintegrins could be utilized to treat integrin-related diseases, including osteoporosis, age-related macular degeneration, metastatic tumors, and obstructive coronary artery disease. We are currently partnered with Allgenesis Biotherapeutics Inc. to design AG-73305, a drug that simultaneously inhibits integrin and vascular endothelial growth factor-associated signal transduction, which is crucial for blocking inflammation, angiogenesis, and fibrosis—key factors in treating retinal diseases. This collaboration with Allgenesis marks the first academic-industry partnership from Taiwan to reach Phase II clinical trials with the U.S. FDA (NCT05301751) for diabetic macular edema using disintegrins. Immunotherapy is a promising approach for cancer treatment. Cytokine-induced killer (CIK) cells demonstrate potent cytotoxicity against various tumors. Interleukin-2 (IL-2) is vital for the immune system and essential for the growth of CIK cells. Its function and expression in the tumor microenvironment make IL-2 and its receptors attractive targets for immunotherapy. In our research, we successfully incorporated a disulfide bond into IL-2 mutants to create IL-2Rα-biased mutants for autoimmune diseases and IL-2Rβγ-biased mutants for cancer. We anticipate that the IL-2 and disintegrin mutants developed in this study may enhance the treatment of hematologic and solid tumors, especially when combined with other therapies.

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Current Position/Affiliations

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Education/Training

1991 Ph.D. Department of Chemistry, Florida State University, USA

Professional and Research Experience

2023 – 2025, Executive Vice President, National Cheng Kung University, Taiwan.

2020 – 2023, Assistant Vice President, National Cheng Kung University, Taiwan.

2017 – 2019, Director General, Department of Life Sciences, Ministry of Science and Technology, Taiwan

Awards and Honors

2024, Outstanding Team Award of National Biotechnology Research Park, NBRP Pitch Day

2022, Gold Medal of National Invention and Creation Award

2016, Outstanding Research Award of MOST

2016, Outstanding Technology Transfer Award of MOST

2014, Honorary Scholar Award of K.T. Li Foundation

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Selected Publication

Wang, Y.-T., Chang, Y.-T., Huang, C.-H., Chen, C.-Y., and Chuang, W.-J.* (2026) “Structural differences of rhodostomin and trimucrin in recognition of integrin αvβ3”, Commun Biol. Accepted.

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