Clofazimine biocrystals and immunomodulation

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Clofazimine (CFZ) is a clinically useful antibiotic on the WHO's list of essential medicines for the treatment of leprosy. Since its initial use in 1969, CFZ has cured over 16 million leprosy patients with no reports of drug resistance. Therefore, with the global emergence of drug-resistant microbials, CFZ has received renewed interest. In mice, as in humans, orally administered CFZ is actively sequestered as a mechanism of drug detoxification by tissue resident macrophages, where it is mostly found as intracellular crystal-like drug inclusions (CLDIs). Although there have been several reports of CFZ immunomodulatory action, the underlying mechanism for this property is mainly unknown. With the purpose of elucidating immunomodulatory mechanisms, our studies have shown that CLDI's possess functions that include the downregulation of Toll-like receptor expression and pro-inflammatory pathways, while upregulating anti-inflammatory pathways in macrophages without exhibiting toxicity. Furthermore, with the use of well-established animal injury models (lung and foot) we have shown that CLDIs are associated with increased IL-1RA production, leading to profound systemic anti-inflammatory activity. In light of new knowledge on the safety and activity of CLDIs, we are currently researching into the reformulation and repurposing of CFZ as synthetic CLDIs for the treatment of inflammatory disorders such as COPD and rheumatoid arthritis.

Biography

Gi Sang Yoon has completed his PhD from Wayne State University in Cell Biology and Anatomy. He is currently investigating the mechanisms of drug sequestration and accumulation, and elucidating drug mechanisms of action with the goal of reformulating and repurposing clinically successful drugs as part of his postdoctoral studies at the University of Michigan College of Pharmacy. He has published numerous papers in reputed journals and has been serving as a reviewer for two journals.

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