Trends in Natural Product Research – PSE Young Scientists' Meeting
Budapest, June 19th-21st, 2019
PFP
doi: 10.14232/tnpr.2019.pfp

Natural compound inducers of immunogenic cell death

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Accumulating evidence documents the anticancer potential of the immune response that can be re-established by modulating the immunogenicity of dying cancer cells. This regulated cell death process is called immunogenic cell death (ICD) and constitutes a new innovating anti-cancer strategy with immune-modulatory potential thanks to the release of damage-associated molecular patterns (DAMPs). Some conventional clinically-used chemotherapeutic drugs as well as preclinically-investigated compounds of natural origins such as anthracyclines, microtubule-destabilizing agents, cardiac glycosides or hypericin derivatives possess such an immune-stimulatory function by triggering ICD. In this review, we summarize the effects of ICD inducers on DAMP signaling leading to immune recognition. We will discuss potential strategies allowing to overcome resistance mechanisms associated with this treatment approach as well as co-treatment strategies to overcome the immunosuppressive microenvironment. We will highlight the potential role of metronomic immune modulation as well as targeted delivery of ICD-inducing compounds with nanoparticles or liposomal formulations to improving immunogenicity of ICD inducers aiming at long-term clinical benefits.

Acknowledgements

MD's research at SNU is supported by National Research Foundation (NRF) [grant number 019R1A2C1009231] and by a grant from the MEST of Korea for Tumor Microenvironment Global Core Research Center (GCRC) [grant number 2011-0030001]. Support from Brain Korea (BK21) PLUS program and Creative-Pioneering Researchers Program at Seoul National University [Funding number: 370C-20160062] is acknowledged. MD also thanks the "Recherche Cancer et Sang" foundation, "Recherches Scientifiques Luxembourg" association, "Een Häerz fir kriibskrank Kanner" association, Action LIONS "Vaincre le Cancer" association and Télévie Luxembourg.

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