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Targeting aryl hydrocarbon receptor (AhR) to discover new pathways and drugs with anti-inflammatory properties to treat autoimmune diseases

Aryl hydrocarbon receptor (AhR) plays a central role in mediating detoxification induced by chemicals. Interestingly, recent studies have demonstrated an exciting new role for AhR in the regulation of of inflammation and autoimmune diseases. Also, chronic inflammation is considered to be the underlying cause of most clinical disorders including autoimmune, cardiovascular, neurodegenerative diseases, obesity, as well as certain types of cancer. Thus, developing novel anti-inflammatory drugs can have major impact on health, worldwide. Numerous endogenous and plant derived products are AhR ligands. Resveratrol (RES; 3,5,4'-trihydroxystilbene), a nonflavonoid polyphenol found in mulberries, peanuts and grapes. Our laboratory has done pioneering studies identifying that RES activates AhR to exhibit anti-inflammatory properties. We have tested the effect of RES on a number of inflammatory and autoimmune diseases including multiple sclerosis, staphylococcal enterotoxin B-induced lung inflammation, vascular inflammation, colitis, and diabetic embryopathy. We have noted that RES triggers multiple pathways of immunomodulation to suppress inflammation including induction of apoptosis through upregulation of Fas and FasL in activated T cells, induction of myeloid-derived suppressor cells (MDSCs), regulation of SIRT 1 and NFkB pathways, as well as p53 and phosphorylated p53. Because the underlying inflammatory pathways that trigger autoimmune diseases constitute diverse elements such as effector Th1 and Th17 cells and cytokines, innate immunity, autoantibodies, FoxP3+regulatory T cells and MDSCs, from the therapeutic viewpoint, compounds such as RES that activate AhR are ideal because of their diverse modes of action. (Supported by NIH grants: R01 AT006888, R01 ES019313, R01 MH094755, P01 AT003961, P20 RR032684).

Biography

Prakash Nagarkatti, Ph.D. is currently the Vice President for Research at the University of South Carolina. He is also the Director of the NIH Center for Inflammatory and Autoimmune Diseases for $6 million, and the Director for Dietary Supplements and Inflammation for $10 million. Dr. Nagarkatti has published over 160 scientific papers and has trained over 28 graduate students, 16 post-doctoral fellows and 17 junior faculty. He has won numerous awards nationally and internationally and has several patents. Currently he oversees $238 million in sponsored research at USC. He has chaired and served as a member on numerous NIH Review Panels.

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