Mechanism for Myeloma Advancement, Resistance to Drugs Discovered by Keck Researchers

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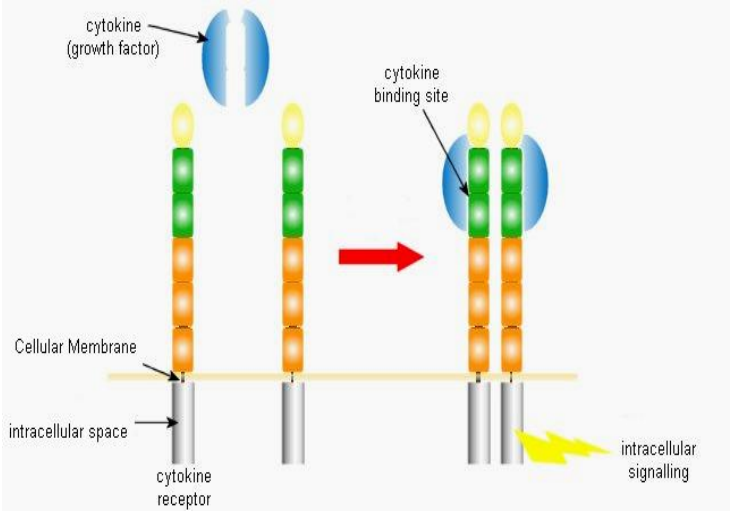
Cancer is the second-leading cause of death for adults in the United States. Multiple myeloma, a bone-marrow cancer that accounts for 10% of all blood-borne malignancies, is considered particularly incurable. Myeloma has such a high fatality rate because it is particularly aggressive and difficult to treat. Dr. Preet Chaudhary and his research team at USC's Keck School of Medicine may have found a mechanism to account for these characteristics.

Myeloma and IL6

Cancer cells are driven by growth factors that encourage their multiplication and survival. In the case of myeloma, cytokine IL6 has been implicated. A quick review of cellular biology: cytokines are small proteins involved in intercellular signaling. Each cytokine has a receptor on the surface of the cell. When it binds to this receptor, the result is a cascade that has effects on cellular function.



This is the same process that allows hormones to affect the cells throughout the body. Understanding the general function of cytokines helps explain the importance of

IL6's involvement in the growth of myeloma cells. Myeloma cells are particularly depended on IL6 for growth and survival during the early stages of the disease. Independence from IL6 indicates an advance in the disease's progression as it spreads throughout the body. Further, myeloma is particularly resistant to the drug used to treat it, called dexamethasone, as well as other drugs being designed to replace this ineffective drug.

IL6 Role in NF-κB Pathway

Dr. Chaudhary and his team looked to this unusual behavior of myeloma cells for their inspiration. Dr. Chaudhary had previously found a protein called K13 that activated a pathway called NF-κB, which is usually involved in the inflammatory and immune responses and in cellular survival and proliferation. The researchers first performed several experiments to confirm the role of IL6 in myeloma growth and survival. Once this effect was confirmed, researchers then looked to the NF-κB pathway. Abnormalities in this pathway, once activated, promote the survival of the myeloma cells. The activation of the pathway alone is enough to initiate IL6 independence in myeloma cells, which signals a major advance in the course of the disease and may explain this particular cancer's aggressive nature. NF-κB activation was also shown to be associated with the protective effect of K13, which was the cause of the pathway's protective affects on IL6-withdrawal cell death. In short, activating NF-κB bypasses IL6.

Let's Cure Myeloma!

Finding a way to inhibit the NF-κB pathway could increase the success of treatments for multiple myeloma. Inhibiting the pathway could prevent the diseases progression and allow for treatment of previously hopeless cases. Myeloma would not longer be incurable. It could also spell a way to treat other cancers, like lymphoma, where IR6 is the growth factor. Further research for this team will include looking for potential chemicals to inhibit this pathway. This discovery could be a promising advance in cancer research and treatment for one of the most aggressive cancers.