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Interleukin-6 in multiple myeloma and related plasma cell dyscrasias.

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Since the discovery a decade ago that interleukin-6 is a growth factor for human multiple myeloma (MM) cells, great strides have been made in understanding the relationship of this cytokine to multiple myeloma. A plethora of studies on this topic has confirmed that interleukin-6 is a key growth and survival factor for myeloma cells, as well as a major morbidity factor for patients with MM. There is strong evidence for both an autocrine (in MM cells) as well as a paracrine sources of interleukin-6 induction (from bone marrow stromal cells and osteoblast cells), with bone marrow stromal cells likely serving as the main center of production of interleukin-6 in patients with MM. Moreover, bone marrow stromal cells from patients with MM express viral interleukin-6, a functional homolog of human interleukin-6 that is produced by Kaposi's sarcoma-associated herpesvirus and may further enhance MM cell growth and survival. Soluble interleukin-6 receptor serum levels are elevated in patients with MM; soluble interleukin-6 receptor may amplify circulating interleukin-6 in patients with MM, and complex with interleukin-6, resulting in proliferation of MM cells that either express low or no detectable surface interleukin-6 receptor. Recent advances in our understanding of interleukin-6 signaling cascades mediating MM growth and survival, as well as its impact on cell cycle regulation in MM cells, may lead to therapeutics designed to interfere with these pathways. Finally, considerable progress has been made in identifying and developing agents including antibodies, biologic agents, hormones and drugs that interfere with the interleukin-6 signaling pathways and may therefore have a role in the treatment of MM.