# Bone Marrow Deficits May Explain Blunted CD4 Response

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The suppression and dysfunction of stem cells in bone marrow may help explain why some people don't experience significant CD4 cell increases after starting antiretroviral (ARV) therapy, say the authors of a study to be published in a future issue of *Clinical Infectious Diseases*. The study's authors also suggest that the experimental CD4-boosting drug Proleukin (Interleukin-2, IL-2) may help such individuals.

All immune system cells start out as stem cells generating in our bone marrow. Defects in the production of immune-signaling molecules and the early death of a type of stem cell known as a progenitor cell can ultimately affect the ability of the immune system to develop new cells and respond to infections. Past research has documented damage to bone marrow and stem cells from HIV. No study, however, has thus far examined the bone marrow environment specifically in people who've taken ARV treatment but failed to have a significant CD4 increase—people that researchers have dubbed immunologic non-responders (INRs).

Antonella Isgrò, MD, of the University of Rome Tor Vergata, and her colleagues enrolled 23 people living with HIV who were on ARV therapy. Twelve of the patients were INRs and the other 11 were immunologic responders (IRs)—with robust CD4 responses to treatment. All of the patients in the study had a bone marrow aspiration, which uses a long needle to extract bone marrow fluid and cells, usually from the pelvic bone. These samples from both sets of patients were compared with those from HIV-negative patients.

Isgrò's team found that a group of immune-signaling proteins, specifically tumor necrosis factor alpha and interleukin-7 (IL-7), were much higher in the INRs than in the IRs. These two proteins are associated with suppression of the growth of bone marrow progenitor cells. Conversely, another protein, known as interleukin-2 (IL-2), was much lower in the INRs. IL-2 is associated with growth and expansion of many types of immune cells.

The authors conclude that these signs of cell growth suppression, and increases in signaling proteins that prevent the development of new immune cells in the bone marrow, could explain why INRs don't have a typical CD4 response to ARV treatment. The authors also urge scientists to conduct research using Proleukin or other drugs that may prevent cell death in INRs to determine if the drugs can augment CD4 responses.