# Genetics of aging and cancer resistance

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In the November 15th issue of *G&D,* Dr. Kenneth Dorshkind and colleagues at the David Geffen School of Medicine (UCLA) have identified two genes – p16(Ink4a) and Arf – that sensitize lymphoid progenitor cells to the effects of aging, and confer resistance to leukemogenesis.

Hematopoiesis (the development of blood cells) entails two main pathways: myelopoiesis (the formation of the red and white myeloid cells) and lymphopoiesis (the formation of B- and T-cells). While myelopoiesis remains constant throughout life, lymphopoiesis declines with age.

Dr. Dorshkind and colleagues demonstrated that older B lymphoid progenitor cells preferentially express p16(Ink4a) and Arf, which regulate cell cycle progression to effectively mediate senescence and tumor suppression in these aged cells. In contrast, myeloid progenitor cells consistently expressed much lower levels of these proteins.

The scientists showed that p16(Ink4a) and Arf contribute to the age-related decline in B-cell lymphopoiesis, and that inhibition of p16(Ink4a) and Arf in B-cell progenitors rejuvenates their growth potential and facilitates the development of acute lymphoblastic leukemia.

This newly established role for p16(Ink4a) and Arf linking the proliferative and oncogenic potential of B lymphoid progenitor cells lends genetic insight into the high incidence of lymphoid leukemias in younger patients, as well as the observation that adult leukemias

generally involve the myeloid cell lineages.

As noted by the authors, "In addition to providing a basis for understanding the clinical presentation of lymphoid leukemias, these results raise the possibility that p16Ink4a and Arf may be potential therapeutic targets for rejuvenating the aged immune system".

Source: Cold Spring Harbor Laboratory