Finding protection from tumor growth in unexpected places

June 5 2007

Researchers have discovered that an enzyme commonly involved in regulating blood pressure also provides protection from tumor growth when strongly expressed in immune cells. The related report by Shen et al, “Mice with enhanced macrophage angiotensin-converting enzyme are resistant to melanoma,” appears in the June issue of *The American Journal of Pathology*.

Angiotensin-converting enzyme (ACE) plays a direct role in controlling blood pressure and is a common therapeutic target in hypertension. However, it also plays roles in such diverse processes as fertility, immune cell development, and atherosclerosis, and a few studies have even suggested a role for ACE in generating an effective immune response. In an effort to tease out the role of ACE in immune modulation during cancer, Dr. Kenneth Bernstein’s group at Emory University generated mice (ACE 10/10) that express ACE only in macrophages.

When injected with aggressive melanoma cells, normal mice developed large melanoma tumors whereas ACE 10/10 mice developed only very small tumors. The resistance of ACE 10/10 mice to melanoma growth was confirmed using several different melanoma cell lines and by using different strains of mice expressing high levels of ACE in macrophages. Interestingly, the small tumors of ACE 10/10 mice contained significantly higher numbers of white blood cells, suggesting a large anti-tumor immune response.

To confirm the existence of an ACE-specific anti-tumor immune response, normal mice were depleted of their bone marrow and transplanted with ACE 10/10 bone marrow. When the transplanted normal mice were then injected with melanoma cells, they too were able to control tumor growth. The immune response involved not just the ACE-expressing macrophages but also increased numbers of cytotoxic T cells and levels of immune-activating chemicals and decreased levels of immune-suppressing chemicals. Finally, the ACE 10/10 macrophages alone could direct the immune response and convey protection as direct injection of these cells into melanoma tumors of normal mice yielded decreased tumor size.

Together these studies provide strong evidence that high ACE expression in macrophages produces strong anti-tumor activity. In addition, while most of these studies were performed with melanoma cells, similar results were also obtained with lymphoma cells, demonstrating that ACE-expressing macrophages hold great promise for other forms of cancer. As stated by Shen et al, “If ACE 10/10 mice define a general yet simple means of enhancing immunity, this may be useful to human tumor therapy as well as in other clinical settings.”

Source: American Journal of Pathology