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HERV env: A Targetable Surface Protein in Ovarian Cancer

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Scientific Abstract:

Human endogenous retroviruses (HERVs) are remnants of ancient retroviral infection and compose around 8% of the human genome. These retroviral sequences were thought to lack biological function, but recent advances illuminated their potential physiological and pathophysiological roles. Reactivation of transcription and translation of HERV envelope proteins (env) has been demonstrated in a range of human diseases, including autoimmune diseases and cancers. The therapeutic potential of targeting env proteins has been shown in multiple cancer subtypes, but it is unknown if env is acting as a viral oncoprotein, an agent of immune evasion, a tumor marker, or simply a nonfunctional target expressed on cancer cells against which cancer therapies can be aimed. In ovarian cancer, cell surface expression of numerous classes of HERV env proteins is significantly increased compared to benign ovarian tissue. Further, anti-HERV env antibodies have been detected in the sera of patients with ovarian cancer, but not in matched controls. According to the American Cancer Society, ovarian cancer is the fifth leading cause of cancer deaths among women in the United States. The therapeutic landscape in non- BRCA mutated epithelial ovarian cancer is lacking in specific targeted therapies, and although many women initially respond to chemotherapy, there is a high propensity for disease relapse and chemotherapy resistance. This project will approach HERV env as a therapeutic target or tumor marker for ovarian cancer via techniques in protein engineering, structural biology, and antibody discovery, with the goal of discovering HERV env-specific antibodies for diagnostic or therapeutic indications.

Lay Abstract:

Hundreds of thousands of years ago, before humans evolved from primates, another pandemic caused by viruses occurred. This pandemic was caused by retroviruses, which are viruses that can insert their own genetic information into the DNA of their hosts. Around 8% of human DNA is the remnant of viral genetic material from these ancient infections. These DNA remnants are called human endogenous retroviruses (HERVs). Endogenous means that these bits of viral DNA are now a stable part of our genetic make-up. These retroviral sequences were long thought to be silent 'junk' DNA, but recent research has uncovered the potential for these viral genes to start producing proteins in disease states, such as in cancer or autoimmune disease. For example, in ovarian cancer, researchers have seen that some retroviral proteins stud the surface of ovarian cancer tissues and ovarian cancer cells. In a mouse model of ovarian cancer, a monoclonal antibody treatment targeting a HERV protein slowed tumor growth. According to the American Cancer Society, ovarian cancer is the fifth leading cause of cancer deaths among women in the United States. However, there are few new treatments or diagnostic tools for ovarian cancer. This project will approach HERV proteins as targets for drug discovery with a focus on developing novel monoclonal antibodies to be used either to diagnose or treat ovarian cancer.