Estrogen is responsible for slow wound healing in women

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Estrogen causes wounds in women to heal slower than in men - who have lower levels of estrogen - says a new study published in the April 2012 issue of the FASEB Journal. In the report, scientists from the University of California, Berkeley, provide the first evidence that mild injury response in the eye is fundamentally different in males and females because of estrogen. This discovery provides new clues for successfully treating a wide range of inflammatory diseases such as dry eye disease, rheumatoid arthritis, lupus, multiple sclerosis, and scleroderma.

"We hope that our finding will spur research efforts into delineating sex-specific differences and estrogen regulation of intrinsic circuits that determine the outcome of healthy and routine injury responses," said Karsten Gronert, Ph.D., a researcher involved in the work from the University of California, Berkeley, Vision Science Program, School of Optometry in Berkeley, Calif. "Auto-immune diseases in general are not triggered by a single event; hence, understanding what leads to a recurrent dysregulation of fundamental injury responses may help us treat and/or prevent the development of female-specific diseases."

To make this discovery, Gronert and colleagues administered a mild abrasion injury to the front of the eye of genetically similar male and female mice, and analyzed wound healing by image analysis. To test the role of estrogen, they gave male mice estrogen eye drops and/or drugs that activate specific estrogen receptors. Gene expression of essential enzymes was quantified for the formation of protective lipid signals, specific receptors that mediate their bioactivity, as well as estrogen
receptors in mouse corneas and human/mouse epithelial cell cultures. The formation of protective lipid signals was analyzed by a mass-spectrometry based lipidomic method. They found that estrogen negatively affects a highly evolved protective lipid circuit, called "15-lipoxygenase-Lipoxin A4" that has recently emerged as an important protective pathway in many diseases. This pathway balances the activity of pro-inflammatory signals to promote wound healing and to keep inflammation within safe ranges.

"This study goes a long way to explaining gender differences in inflammation and its resolution," said Gerald Weissmann, M.D., Editor-in-Chief of the FASEB Journal. "It's long been known that women suffer more than men from chronic inflammatory diseases such as lupus or rheumatoid arthritis; this study suggests that estrogen itself is responsible for that difference and pinpoints the molecular pathways that estrogen affects. Molecules that promote the resolution of inflammation show promise as new treatments for autoimmune disease."

Provided by Federation of American Societies for Experimental Biology

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