

Omega-3 polyunsaturated Fatty acids suppress the cystic lesion formation of peritoneal endometriosis in transgenic mouse models.

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Abstract

Omega-3 polyunsaturated fatty acids (omega-3 PUFAs) play a role in controlling pathological inflammatory reactions. Endometriosis is characterized by the presence of endometrial tissue on the peritoneum and an exaggerated inflammatory environment around ectopic tissues. Here peritoneal endometriosis was reproduced using a mouse model in which murine endometrial fragments were inoculated into the peritoneal cavity of mice. Fat-1 mice, in which omega-6 can be converted to omega-3 PUFAs, or wild type mice, in which it cannot, were used for the endometriosis model to address the actions of omega-3 PUFAs on the development of endometriotic lesions. The number and weight of cystic endometriotic lesions in fat-1 mice two weeks after inoculation were significantly less than half to those of controls. Mediator lipidomics revealed that cystic endometriotic lesions and peritoneal fluids were abundant in 12/15-hydroxyeicosapentaenoic acid (12/15-HEPE), derived from eicosapentaenoic acid (EPA), and their amount in fat-1 mice was significantly larger than that in controls. 12/15-Lipoxygenase (12/15-LOX)-knockout (KO) and control mice with or without EPA administration were assessed for the endometriosis model. EPA administration decreased the number of lesions in controls but not in 12/15-LOX-KO mice. The peritoneal fluids in EPA-fed 12/15-LOX-KO mice contained reduced levels of EPA metabolites such as 12/15-HEPE and EPA-derived resolvin E3 even after EPA administration. cDNA microarrays of endometriotic lesions revealed that Interleukin-6 (IL-6) expression in fat-1 mice was significantly lower than that in controls. These results suggest that both endogenous and exogenous EPA-derived PUFAs protect against the development of endometriosis through their anti-inflammatory effects and, in particular, the 12/15-LOX-pathway products of EPA may be key mediators to suppress endometriosis.