

ONCOLOGY
CICINNATI CHILDRENS HOSPITAL

SUMMER RESEARCH OPPORTUNITIES FOR UNDERGRADUATE WOMEN

APPLICATION DEADLINE: 03/01/2018

PROJECT TITLE: Examining passenger mutation vulnerability in Melanoma

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Project Description

Stearoyl-CoA desaturase (SCD) is an endoplasmic reticulum (ER) resident enzyme that catalyzes the rate-limiting step in the formation of monounsaturated fatty acids (MUFAs). The principal product of SCD is oleic acid, which is made by desaturation of stearic acid. Oleate is a major component of membrane phospholipids, cholesterol esters and diacylglycerol. The ratio of stearic acid to oleic acid is critical for the regulation of cell growth and differentiation, as reduction of oleic acid causes loss of membrane fluidity affecting membrane protein localization, signal transduction and gene expression. Its improper signaling has been implicated in many pathologies including cancer.

TCGA data shows that PTEN and SCD are co-deleted in 47% of melanomas. We aim to 1) determine SCD expression levels in five metastatic melanoma lines (A375, 451 Lu, 1205Lu, 852WM, 1232WM);

2) determine cellular viability after treatment with an SCD inhibitor followed by a rescue experiment in the presence of the SCD inhibitor and oleate (the main product of SCD) and 3) test the inhibitor efficacy in metastatic melanoma xenograft models. Nude mice will be injected with melanoma cell lines and treated with the SCD inhibitor upon tumor formation; survival, proliferation and apoptosis indexes will be measured. The SCD inhibitor (CAY10566) is an FDA approved inhibitor for topical use (used for the treatment of acne), so it would be especially beneficial for melanoma patients.