Cody John Paiva – Undergraduate Research 2013

Role of cellular FLIP cleavage during innate immune response to viral infection

Abstract:

Cellular FLICE-like inhibitory protein (c-FLIP) has been identified as a key regulator of caspase-8 activity during programmed cell death (apoptosis). Paradoxically, caspase-8 plays also an essential non-apoptotic role during cell proliferation. More recently it was shown that the caspase-8/FLIP complex is engaged during the innate immunity in response to viral infections. Although it is known that caspase-8 can cleave FLIP, little is known about the regulatory function of c-FLIP in this process. Since innate immunity is the first line of defense against pathogens, it is ourcurrent interest to identifying the role of c-FLIP and its cleavage product., Our preliminary experiments used mouse embryonic fibroblast (MEF) cell lines expressing c-FLIP and its non-cleavable variant D376A as models. The non-infectious RNA molecule poly (I:C), mimicking viral RNA, was used to establish experiments to measure caspase-8 activity and IFN-ß secretion. Now we aim to identify the role of c-FLIP and its variant upon infection of MEFs with coxsackievirus B3.