**Hypothesis and objectives:** Much of the toxicity of crude oil is associated with polycyclic aromatic hydrocarbons (PAHs). Most crude oils contain predominately 2- and 3-ring PAHs (naphthalenes, and fluorenes, dibenzoanthiophenes, and phenanthrenes, respectively), with a small fraction of 4-ring compounds (chrysenes) [1]. Following the 1989 Exxon Valdez oil spill in Prince William Sound, field and laboratory studies with multiple fish species documented a common malformation syndrome, as well as reduced growth and survival to adulthood, induced by embryonic exposure to weathered crude oil [2-5]. Our ongoing studies of PAH toxicity using the zebrafish model demonstrated that the developmental defects associated with oil exposure are (1) attributable to the tricyclic PAH fraction, (2) secondary to direct impacts on cardiac function, and (3) independent of the aryl hydrocarbon receptor/cytochrome P4501A (AHR/CYP1A) pathway traditionally associated with toxicity of high molecular weight PAHs [6-8]. More recently, we confirmed that early cardiac dysfunction is the primary response to oil exposure in embryos of Pacific herring, a native West Coast species [9]. Overall, the phenotypic effects of these compounds suggest multiple myocardial targets including potassium channels, plasma membrane or sarcoplasmic calcium channels, pacemaker currents, or gap junctions. These studies provided novel insight into previously unappreciated cardiotoxicity of the most prevalent classes of PAH compounds. Genetic studies of heart development demonstrate that embryonic cardiac function and morphogenesis are inextricably linked [10]. Therefore, any disruption of cardiac physiology during early developmental stages ultimately impacts the subsequent shape of the heart, which in turn will influence subsequent performance. We hypothesize that the direct cardiotoxic properties of tricyclic PAHs and sublethal influences on heart development are responsible for the reduced fitness observed in grossly normal fish exposed to oil as embryos [3]. At the same time, tricyclic PAH cardiotoxicity may underlie the reduced swimming performance observed in fish acutely exposed to oil [11, 12]. We predict that alterations in cardiac structure due to embryonic oil exposure should also result in reduced swimming performance, and other chronic changes in cardiac physiology. The latter is likely to include altered regulation of the cardiac natriuretic peptides (NPs), a family of hormones secreted by the heart that are key regulators of cardiac function and cardiovascular homeostasis in all vertebrates [13]. NP gene levels are either upor down-regulated in different zebrafish cardiac function mutants [14, 15], and circulating NP levels are altered in a variety of human cardiac pathophysiological states [16, 17]. The diagnostic use of NP levels is currently at the forefront of human cardiology [18, 19]. Our preliminary data suggest that Atrial NP (ANP) levels are upregulated in the zebrafish embryonic ventricular myocardium in response to oil exposure (Fig. 1, Appendix B).

**We propose that sublethal embryonic exposure to weathered crude oil will reduce post-embryonic fitness through measurable influences on cardiovascular physiology, and will test this hypothesis through the following specific aims:**

1. Assess swimming performance and oxygen consumption in larval, juvenile, and adult zebrafish exposed to weathered crude oil as embryos.
2. Characterize changes in gene expression, tissue and blood levels of cardiac natriuretic peptides in response to oil exposure.

Completion of these Year 1 aims will provide the basis for subsequent studies in native West Coast species.