The zebrafish (*Danio rerio*) is increasingly used as a model organism for biomedical research. A unique set of properties (small size, numerous offspring, optical transparency of the embryo and amenability to genetic and chemical screens) has made it an increasingly popular vertebrate animal model among biomedical researchers. It has now become clear that the potential of small fish models far exceeds the fields of developmental genetics, being valuable in almost all biomedical areas, including pharmacology and drug screening.

A particular benefit from the existing technologies in zebrafish arises at the interface between biology and chemistry - the new field of chemical biology. The zebrafish embryo offers unmatched opportunities to identify bioactive molecules in an intact animal. This is particularly relevant in the areas of stem cell research, as these cells can best be studied in their natural environment. Zebrafish are well known for their regenerative capabilities that exceed by far those of mammals. These properties together with the small size of the animals and the availability of many transgenic lines make the zebrafish embryo and larvae an ideal vertebrate system to study the chemical biology of development and regeneration. For example, chemical screens in the zebrafish have already proven their enormous potential by being instrumental in identifying prostaglandins as key components in human haematopoietic stem cell homeostasis (North et al., *Nature* 2007), and identifying a particular class of proteins involved in this regulatory pathway. This protein class is currently being tested in the human clinic.

Thus, we propose that the EU considers the funding of an integrated project where zebrafish researchers and chemists identify and explore novel chemical entities that affect complex cell behavior such as stem cell maintenance, stem cell differentiation, tissue repair and regeneration. This will involve the close interaction of chemists with zebrafish researchers at the European scale pulling expertise in the various areas together. This work will be complementary to ongoing stem cell research using mostly mouse systems or in vitro approaches. Potential areas of interest are development and regeneration of the central and peripheral nervous systems, the retina, the heart and appendages but also the control of the immune response in the repair processes and the transformation of stem cells into cancer cells.

The benefit for European research, industry and health care would be enormous. It has increasingly been recognized that existing drug screening paradigms are becoming less effective. For example since 1997 the Food and Drug Administration (FDA) in the U.S. has witnessed a 50% drop in the registration of newly discovered pharmaceuticals. The demand for novel therapies and drugs in the area of stem cell control will increase massively with the aging of European populations. Thus the proposed integrated project will target several key issues of high priority bringing European excellence in the fields of chemistry together with developmental biology using the zebrafish as an innovative discovery tool.