

Lawrence E. Harrison, MD

Anti-cancer effects of phenylbutyrate

[This proposal will evaluate the mechanism and therapeutic potential of phenylbutyrate for treating colorectal cancer]

Colorectal cancer is the third leading cause of cancer deaths in the United States. Cytotoxic chemotherapy has been used to treat patients with advanced colorectal cancer with limited success, often at the expense of severe side effects. Therefore novel chemotherapeutic approaches are needed. An alternative to traditional chemotherapy is differentiation therapy, which offers “rehabilitation” to cancer cell rather than traditional chemotherapy’s “retribution.” Differentiation drugs uses the cell’s own mechanisms to cause a malignant cell to stop growing. However, prior to clinical application of differentiation therapy, a more detailed knowledge of how these agents promote cell differentiation is important.

Recent reports suggest that the compound, *phenylbutyrate* is an effective differentiation drug in a variety of cell types, including brain tumors, prostate cancer, leukemia and melanoma. The appeal of phenylbutyrate as an anti-cancer drug is that it is non-toxic, can be taken in an oral form and can safely achieve therapeutic blood levels in humans. The overall goal of this project is to evaluate the therapeutic potential of phenylbutyrate for treating colorectal cancer. Specifically, the objective of this proposal is to achieve a better understanding of the mechanism of phenylbutyrate-induced differentiation. This is important, since this study will guide the development and the use of phenylbutyrate clinically, as well as additional differentiation agents for potential cancer therapy and cancer chemoprevention.