CHAPTER III

OBJECTIVES

In many tumors, dysregulation of apoptosis plays a major role in the pathogenesis of tumor development. Apoptosis is believed to be one of the main cellular mechanisms by which chemotherapy and radiation therapy kill cancer cells. Unfortunately many forms of cancer, including cholangiocarcinoma, are resistant to cancer therapy. One way to develop resistance to radio- and chemotherapy is the ability of tumor cells to inhibit the endogenous suicide program or apoptosis. Apoptosis can also be stimulated by death receptors, including the TNFR superfamily. TNF receptor is an important member of the death receptor family that shares the capability of inducing apoptotic cell death. Besides this apoptotic signaling, TNF receptor also has the ability to transduce cell survival signals. Although signaling pathways are well-defined nowadays, the sensitivity/resistance response in cholangiocarcinoma is still poorly understood.

Understanding how cholangiocarcinoma responds to apoptosis after TNF-alpha treatment may assist in finding potential therapeutic targets.

Therefore, this study addresses the effects of TNF-alpha on apoptosis of cholangiocarcinoma. Two CCA cell lines were used as models: KKU-213, a well-differentiated CCA cell line and KKU-100, a poorly-differentiated CCA cell line. The investigation consisted of the following methods:

Part I: Characterization of the expression of TNFRI and TNFRII of KKU-100 and KKU-213 using RT-PCR

Part II: Determination of the effects of TNF-alpha on critical apoptotic features of KKU-100 and KKU-213 using MTT assay, DAPI staining and PARP cleavage