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Cellular Level Diagnosis of Duodenal Adenocarcinoma: First Step in Early Diagnosis

Abstract:

Duodenal adenocarcinoma (DA) is a rare form of gastrointestinal cancer that leads to death. DA is asymptomatic and have non-specific symptoms such as stomach pain, fatigue, weight loss, and nausea[2]. Endoscopy is used as a diagnostic modality[2]. The long-term goal of the study would be to identify symptoms associated with DA so early treatment plans would be available.

There are varying expressions that have been associated with DA such as high expressions of CDX2 protein and Mucin1 (MUC!) glycoprotein, which is associated with a poor prognosis in patients with DA[7,9,10]. This leads to the hypothesis that increased protein expressions of CDX-2 and MUC1 leads to changes in cell structures that cause duodenal adenocarcinoma.

The proposed research will focus on looking at the histology of DA to find high expressions of proteins and specific symptoms or signs associated with the highly-expressed proteins in the patients. Mass spectrometer will be used to find abnormal expressions of proteins in the tissue samples of the DA patients. Once a specific type of protein expression is ensured, cell morphology of the cells with overexpressed proteins using electron microscopy to find cellular level diagnosis.

The long term goals would be to develop a timeline of cancer development from stage I to stage IV in patients with DA. The proposed research will impact the diagnosis of DA and cellular level signs associated with DA for early diagnosis and prevention.

Aims:

Overexpression of proteins are thought to be associated with the cause of duodenal adenocarcinoma, a rare type of small intestines cancer. Duodenal adenocarcinoma (DA) has non-specific symptoms that makes it hard to diagnose. On the cellular level, DA has been associated with overexpression of homeobox protein CDX2 and glycoprotein Mucin 1 (MUC1). CDX2 protein is associated with differentiation of the intestines in the embryonic stage and regulates intestinal homeostasis in adults[3]. Another study showed an overexpression of glycoprotein MUC1 leads to rigid cell structure and larger molecular size of the cell surface[5]. The two proteins mentioned are associated with other forms of cancer such as colorectal cancer and breast cancer. So far, no research has performed mass spectrometry on duodenal adenocarcinoma tissues to find specific protein overexpression, making it difficult to determine the proteins associated with the cancer development.

The goal of this proposed research is to easily identify early prognosis of DA by collecting epithelial cells from the duodenum of patients and by performing mass spectrometry to find signs of abnormal protein levels. Since DA lack specific symptoms other than a tumor in the duodenum, it is better to look at a cellular level for early diagnosis and prevention. Cellular changes are expected to occur by overexpression of CDX2 and MUC1 proteins. A timeline of the

cancer development can be created with the proposed research, offering guidelines for prevention and treatment.

Aim 1 will establish a common protein overexpression associated with DA. Based on previous studies, CDX2 and MUC1 protein expressions will be tested and looked for using matrix-assisted laser desorption/ionization (MALDI) mass spectrometry[5]. Depending on the stage of the cancer development, the level of overexpression of the proteins will be measured. The overexpression of the proteins will generate an expression associated with DA and the timeline of the development of DA-associated proteins.

Aim 2 will examine the cell morphology of the epithelial cells with the overexpression of the proteins found in the DA cancer cells. Transmission electron microscope (TEM) will be used to look at the morphology of the cancer cell. Cell morphology associated with CDX2 and MUC1 will be observed and this will qualitatively determine the development of duodenal adenocarcinoma.

The proposed study will introduce a new diagnostic guidelines for DA and will give greater insight to the signs for DA at a cellular level. Overexpression of CDX2 and MUC1 proteins will cause DA, which in turn cause changes in the cell structure of the cancer cells. The findings of the proteins and the cell structure will provide early diagnosis for DA as well as cancer development timeline that will be useful in determining the treatment for DA depending on the cancer stage.

Background and Significance:

Duodenal adenocarcinoma (DA) is a rare form of small intestinal cancer with low 5-year survival rates. DA has often been grouped together with colorectal cancer because of lack of research and information about the cause of DA[2]. One of the way to treat DA other than chemotherapy is to perform surgery to remove the tumor or metastasized organ. In stages III and IV, surgery did not significantly increase the survival rates of the patients[1]. Expression CDX2 has been associated with colorectal cancer and it has also been shown in DA[8]. A research showed poor prognosis associated with MUC1 glycoprotein[9]. The research used antibody to examine the association of the MUC1 expression in the cancer cells. A specific strain of human cancer cell line was used in the research. It also turns out that not every patient showed an expression for MUC1. This lead to my experimental method of using mass spectrometry to find specific proteins associated with DA. Mass spectrometry is useful in identifying proteins and the level of expression, making it easier to find which proteins are overexpressed. In addition to mass spectrometry, electron microscopy will be used to look at the cell structure and how overexpression of a certain protein affects the cell morphology[4]. This can determine the diagnostic signs for DA. The next step for this proposed research would be to develop a standard to diagnose patients with DA since DA is not known to be hereditary. So the family members of the patients with DA could also be tested to look at the hereditary association with DA.

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