Chapter 2

Aims and Objectives

1. Identification and validation of differentially expressed transcripts in gastric adenocarcinoma using DNA microarrays
2. Identification and validation of secreted proteins differentially expressed in gastric cancer using mass spectrometry

Specific aim 1: Identification and validation of differentially expressed transcripts/mRNAs in gastric adenocarcinoma using DNA microarrays

Rationale

Oncogenesis is a multistep process marked by aberrant molecular changes leading to transformation and malignancy\textsuperscript{133}. Discovering these aberrations would lead to a better understanding of the disease. Gastric cancer is one of the highly prevalent cancers in Asia both in men and women\textsuperscript{2}. It is an aggressive malignancy associated with very poor prognosis\textsuperscript{134}. Delineation of the mechanisms leading to the development of tumors would facilitate discovery of molecular markers for early diagnosis, treatment and prognosis. Though, several studies have been carried out on gastric cancer, it still remains challenging to identify suitable molecular markers. More studies are warranted at different population and geographical locations to identify appropriate markers for disease diagnosis and prognosis. This study was carried out with this background to discover novel markers for gastric cancer. Microarray-based gene expression profiling of gastric adenocarcinoma tissues and adjacent non tumor tissues was performed to identify aberrantly expressed transcripts.

Specific aim 2: Identification and validation of secreted proteins differentially expressed in gastric cancer using mass spectrometry

Rationale

Plasma is considered as an attractive source of biomarkers since it harbors proteins released from various organ systems. Proteomic profiling of plasma from cancer patients is one of the most commonly used approaches to identify circulating markers pertaining
to a specific cancer\textsuperscript{135}. However, the mainstay in analyzing plasma is its complexity in terms of protein diversity and dynamic concentration range up to ten orders of magnitude. A recent strategy that has been proposed to overcome this limitation is to study the conditioned media of cell lines termed as secretome which is enriched with secreted or shed proteins due to its proximity to the tumor cells\textsuperscript{126}. The secretome as compared to plasma is not so complex which increases the likelihood of identifying proteins affected in particular cell type. Targeted studies can be further carried out to validate the identified secreted proteins for its presence in serum. With this background, the current study was aimed at profiling the gastric cancer secretome using gastric cancer cell lines.