Chapter 2

Objectives:
Head and Neck Squamous cell carcinoma (HNSCC) is one of the leading causes of cancer related deaths worldwide and especially in India. Majority of HNSCC cases are diagnosed in the late stages when surgical intervention is the only mode of treatment in conjunction with chemo- and/or radiotherapy. The most prominent symptom the HNSCC patient presents with is dysphagia. Currently, there are no reliable tumor based markers which can be used for early diagnosis and prognostication of ESCC. More importantly there are not many studies till date which have tried to identify differentially expressed proteins of HNSCC. This prompted us to carry out a series of studies to identify differentially expressed proteins as markers for HNSCC. Hence, in this thesis I have proposed to identify differentially expressed proteins in HNSCC secretome and total proteome.

1. What is the global protein expression profile and which are the major differentially expressed proteins in HNSCC secretome?

2. What is the expression pattern of some key differentially expressed proteins identified in our secretome analysis in a large cohort of HNSCC patients?

3. What is global protein expression profile of HNSCC cells and which are the major differentially expressed proteins in HNSCC.

4. What is the functional role of potential markers in chemoresponsiveness against cisplatin and 5-Flourouracil drugs?

The study is subdivided into two parts and the corresponding objectives are outlines as follows

Specific aims of Part 1
1A. Differential proteomic analysis to identify secreted protein markers from non-neoplastic and neoplastic HNSCC cell lines using Isobaric Tags for Relative and Absolute Quantitation (iTRAQ)-based quantitative proteomic approach

1B. To validate the expression of secretome based markers using immunohistochemistry in a large cohort of HNSCC cases

**Specific aims of Part 2**

2A. Differential proteomic analysis of HNSCC cell lines to identify dysregulated proteins in HNSCC

2B. Validation of candidate proteins by western blot analysis and immunohistochemistry.

2C. Assess the role of the candidate proteins in the sensitivity of HNSCC cell lines to cisplatin and 5-FU