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# E2F Transcription Factor 1 and its Role in the Cell Cycle and Tumor Suppressor Proteins

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# E2F Transcription Factor 1 and its Role in the Cell Cycle and Tumor Suppressor Proteins

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## ABSTRACT

**E2F Transcription Factor 1 (E2F1)**

E2F1 is a transcription factor, in which its expression is increased in human cancers. “Transcription factor E2F1 binds to and activates transcription,” in return leading to increased transcription at the G1 and S phase of the cell cycle (Slansky). The E2F transcription factor family “plays a crucial role in the control of cell cycle and action of tumor suppressor proteins and is also a target of the transforming proteins of small DNA tumor viruses” (NCBI).

## BACKGROUND

Eukaryotes, such as humans and animals, are made up of their own set of unique and distinguishable chromosomes. Chromosomes are made up of chromatins, which consists of proteins, RNA and DNA. Strands of DNA (deoxyribonucleic acid) are surrounded by histones, which are categorized as proteins that are essentially found in the nucleus of eukaryotic cells. Histones are subject to modifications, such as methylation, which will directly affect the gene expression in DNA.

***What is lysine methylation?***

Histone modification, such as lysine methylation, occurs on histones H3 and H4. Methylation occurring in lysine residues are catalyzed by enzymes. “Each of these lysine side chains can be mono-, di- or trimethylated” (Martin). What is unique in lysine methylation is that it is able to signal either an activation or repression depending on the site in return, turning certain genes on or off in a gene expression. “Methylation on the same site can lead to different outcomes depending on the number of methyl groups added” (Martin).

***What is the role of lysine methylation in E2F1-induced apoptosis?***

Lysine methylation of histones plays an essential role in the complex transitions of chromatin structure, “which regulate[s] the accessibility of transcription factors to nucleosomal DNA” (Kontaki). Histone lysine-methyltransferases regulates specific gene expressions through the methylation of transcription factors, such as E2F1. Methylation at lysine-**K185** stimulates degradation of the protein, and can have opposing biological outcomes.

## PURPOSE OF STUDY

Histone lysine methylation serves an array of important functions. In the past few years, studies on different organisms have resulted in the identification of several enzymes that catalyze site-specific histone lysine methylation. The characterization of these enzymes has revealed important functions of histone methylation in many different biological processes that range from heterochromatin formation to transcription regulation.

## METHODS

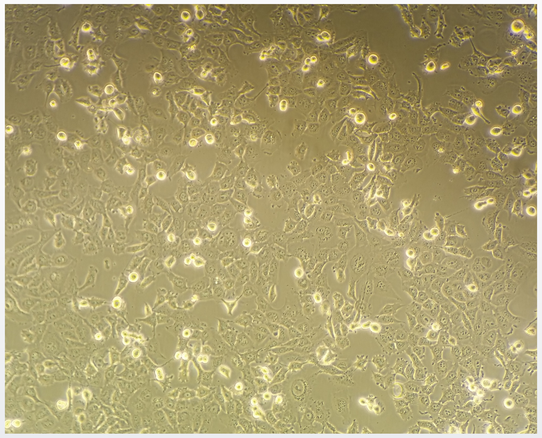

*Figure 1: Specimen of a small cell lung carcinoma via microscope*

**Immunoprecipitation**

By using the specificity of antibodies, immunoprecipitation (IP) isolates target proteins, such as antigens, out of sample mixtures (Kaboord). IP typically tests for protein to protein interactions and is responsible for the lysis of cells (or lysates).

In a small cell lung carcinoma specimen, a lysis buffer is used to break down a cell’s wall in order to burst the cell and reveal the proteins that are inside. In addition, a Tris wash buffer is used to maintain a pH of 7.4. This keeps the proteins at the right pH, which is relatively neutral and close to the pH level of blood.

A detergent called sodium dodecyl sulfate (SDS) is added to denature the lysates. Once all of the proteins are separated in the solution, the lysates are put in a tube and centrifuged. DNA, RNA, and pieces of the cell wall are discarded, while the top layer of protein is utilized. Immediately after denaturation, protease inhibitors are added to stop protein from degrading since protein degrades quickly, the cells are put into an ice bath to chill.

Lastly, antibodies derived from rabbit blood are added to the lysates in order for the antibodies to bind to the protein beads (antigens). These steps are repeated until the protein of interest is found.

**Western Blot**

Immunoprecipitation (IP) is used to prep for Western Blotting. Western Blot uses antibodies to detect proteins that have been separated by electrophoresis gel. The protein that is retrieved from IP runs through a gel, which separates the proteins depending on size and shape. The purpose of Western Blotting is to test for a binding partner. For example, primary antibodies are able to bind to square proteins that are needed in the cell cycle. Once an antibody binds to a protein that specific binding is confirmed.

## METHODS


*Figure 2: Western Blotting detects proteins that have been separated by electrophoresis gel.*

## RESULTS

Lysine methylation alters the amino acid number in a histone. Each protein has its function, and its function is regulated in many ways. Through epigenetics, a lung cell is able to turn into a liver cell by changing the modifier. Transcription factors, such as E2F1, modify and revolutionize the realm of epigenetics.

## CONCLUSIONS

A cancer cell’s metabolic pathway is damaged. In varied cancer stem cells, proteins that do not typically interact with each other end up interacting with each other, and that is what starts the proliferation of tumor masses. Due to the complex and ever-growing nature of cancer research, further and developing studies will be made in the years to come. The results will pave the way to many studies regarding cancer and how to target it at its root.

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