Initiating Cell Division: The Role of the Ternary Complex

Whitefish Bay High School SMART Team
Zixiao Chen, Youngjoon Choi, Justin Fenzl, Anna Gibson, Alison Huckenpaler, Zak Kaplan, Tim Murray, Sam Roth, Martin Steren
Mentors: Ravi Misra, Ph.D. and Mary Holtz, Ph.D. Medical College of Wisconsin
Teachers: Judy Weiss, Marisa Roberts

**Abstract**

DNA, the fundamental building block of cells, tells the cell how to produce proteins, regulate cell division, and pass genetic information from parent cell to daughter cell. However, a human’s DNA is over three billion base pairs long, and transcribing the entirety of the DNA to get a duplicate of a small section is highly inefficient. To combat this, DNA contains specific sequences that work in conjunction with proteins to signal where to begin and end copying for a specific section. One such sequence of nucleotides is the Serum Response Element (SRE). The SRE is bound by a protein called Serum Response Factor (SRF). SRF binds as a dimer to the minor groove of DNA. SRF, in combination with SAP-1, another protein, bind to DNA at the SRE. The SAP-1 protein contains two parts: the SAP-1 box that binds to SRF, and the SAP-1 ETS domain that binds to DNA. These two parts are linked with a flexible chain of amino acids. Together, SRF and SAP-1 form a ternary complex with DNA that marks the DNA for transcription. SRF regulation of gene transcription plays an important role in embryonic development, possibly aiding in heart development. Mouse embryos devoid of SRF die early in development, never coming to term. When transcription of the mRNA is misregulated, SRF can cause cancer. This specific ternary complex binds to a portion of the genome that starts the transcription of the human c-fos proto-oncogene when the cell is externally stimulated. Research on this complex is still continuing and scientists are getting closer to understanding its full potential.

**Step 1**
Epidermal growth factor (EGF) binds to growth factor receptor (EGFR) in the membrane, initiating a conformational change in the receptor, causing the intracellular portion of the receptor to become phosphorylated.

**Step 2**
Phosphorylation (the Signaling Cascade), initiates a chain reaction which carries down through the enzymes MEK 1&2 and ERK 1&2.

**Signalizing Cell Division**
Epidermal growth factor (EGF) signals a cascade of reactions that enables the proteins SRF and SAP-1 to come together and bind to a specific sequence of DNA referred to as the SRE. This interaction with DNA initiates the transcription of target genes, thus eliciting a cellular response to the EGF signal. EGF signals the cells to grow and divide in order to heal a wound. However, it is also through this process that tumors are formed. Tumors are large masses resulting from uncontrolled cell growth, which may result from an abnormality with the EGF signaling process.

**Step 3**
ERK1 and/or ERK2 pass through the nuclear pore and activates Serum Response Factor (SRF) to combine with SAP-1, forming the Ternary Complex Factor (TCF).

**Step 4**
TCF binds to the DNA at the SRE sequence of the target gene, fos, which signals RNA polymerase to bind to the fos gene.

**Step 5**
RNA polymerase goes to TATA box of the fos gene and begins to transcribe the gene and make the mRNA encoding the fos protein.