Summary: The Dual Nature of Transforming Growth Factor ß

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The pleiotropic roles of transforming growth factor beta in homeostasis and carcinogenesis of endocrine organs

Markus Fleisch, Christopher A Maxwell, and Mary-Helen Barcellos-Hoff. *Endocrine-related Cancer*. 2006 Jun;13(2):379-400.

Definitions

Apoptosis-A normal and active process of cell death characterized by cell shrinkage, DNA condensation and DNA degradation. Also referred to the programmed cell death of abnormal cells.

TGFß- Secreted by many different cell types, stimulates wound healing but in vitro is also a growth inhibitor for certain cell types.

p53-A tumor suppressor gene that is frequently inactivated or mutated in tumors and transformed cells and is able to cause potentially cancerous cells to destroy themselves. When the p53 gene has been damaged or altered, p53 loses its ability to block cell growth.

Genes-Genes are pieces of DNA that form hereditary units passed from parent to offspring. Genes are the DNA templates that code for proteins. A gene occupies a specific position on a chromosome. Genetic alterations or mutations are associated with breast cancer risk. The two main types of genes that are now recognized as playing a role in cancer include *oncogenes* and *tumor suppressor genes*.

Background

Transforming Growth Factor ß (TGFß) is a pervasive signaling molecule which plays a critical role in several pathways involved in regulating cellular and tissue homeostasis. TGFß demonstrates both tumor suppressive and tumor promotive properties and the dual nature of TGFß makes it a very complicated molecule to study.

Investigations

This review outlines current knowledge of TGFß signaling and regulation of cell-cycle while emphasizing the dual role TGFß plays in tumor growth and malignancy.

Results

TGFß-signaling: TGFß regulates the expression of over 100 genes. Such involvement demonstrates the profound roll it plays in cell-cell signaling and genetic expression.

Regulation of cell-cycle: TGFß regulates p53, a tumor suppressor protein responsible for eliminating damaged, potentially carcinogenic cells. TGFß is regulated by hormones on a cyclic cycle and is responsible for controlling growth.

Dual role in cancer: During the initial stages of carcinogenesis, TGFß acts as a tumor suppressor by initiating apoptosis and maintaining chromosomal stability. In the later stages of tumor progression however, TGFß acts as a tumor promoter by advancing the rate of migration and metastasis.

	Early Stages	Late Stages
▪	▪ Restricts abnormal proliferation ▪ Protects against tumorigenesis ▪ Inhibits growth	▪ Promotes abnormal proliferation ▪ Promotes tumorigenesis ▪ Disrupts the stroma ▪ Facilitates metastasis

Discussion

The importance of TGFß in both the positive and negative regulation of tumorigenesis has been gradually revealed, offering new insight into the communication system of the mammary microenvironment. The relatively recent appreciation of its role in modulating hormonal responses offers a new perspective on its differential mechanisms. The dual nature of TGFß makes it very difficult to pinpoint where and how it is affecting the development of cancer.

Implications for Future Research

The broad range of complex timing events associated with TGFß makes a complete understanding of its mechanistic action elusive. As such, the timing and duration of TGFß therapeutic intervention is critical. Further exploration is anticipated to reveal valuable information.