

Genia: A system facilitating the search for therapeutic targets.

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A cell receives a great number of chemical signals generated in the milieu, by other cells or from within themselves. These regulate their metabolism, determine their differentiation, and indicate when to divide or to start a death process. The signals are often transmitted to the genes through receptors participating in diverse transduction pathways. They can converge or branch out to give rise to others creating a complicated interconnected network not easily comprehended by simple visual inspection.

In this work we present recent progress with **Genia**: an expert system which has Ras signal transduction pathways. In order to analyze the transduction pathways in a network where great amount of components is involved, it is necessary to utilize computational systems, which simplify the task. Expert systems are an application of the artificial intelligence that uses a knowledge base supplied by a human expert to solve problems. The degree of the problem solution depends on the quality of the data and rules made by the human expert.

In particular, we have been interested in the Ras signal transduction pathways, as it is a key protein in the amplification of the signal induced by the growth factors. It is coded by ras, a proto-oncogen associated with different types of cancer. Proto-oncogenes are genes whose mutations result in oncogenes. An oncogene protein product has abnormal activity and/or it express in abnormal levels, which leads to a cell death or gives rise to a cancer.

The transforming ability of Ras varies in the different types of cancer depending on its frequency of mutation. For example in cases of pancreatic cancer 95% is mutated, in leukemia 30% and in breast cancer 5%.

We have identified protein 14-3-3 as a potential therapeutic target and we have chosen the use of triplex forming oligonucleotide (TFO) to inhibit this gene transcription in order to test if it could aid in chemotherapy and radiotherapy as coadjuvant in stimulating cell dead. We have synthesized the TFO's and experimentally determined the formation of triplex in vitro.