Triplex DNA Analysis and Probe Design Using Constraint Logic Programming

Zhuan Chen and Anthony Kusalik
zhc134@cs.usask.ca kusalik@cs.usask.ca
Computer Science Department, University of Saskatchewan, Canada

Calmodulin (CaM) is known to act as the main regulator of Ca^{2+}-dependent signaling in eukaryotic cells. It is involved in the regulation of a wide variety of fundamental cellular processes including intermediary metabolism, muscle contraction, and cell division [Vand94]. The human genome has three *CaM* genes. Transcriptional inhibition is one method for studying the regulation of expression and function of *CaM* genes. Triplex DNA technology can inhibit transcription of a specific gene via a triplex DNA interaction between a synthesized DNA oligonucleotide and a specific DNA promoter region of the gene [Chan97]. When multiple genes exit, a well-designed triplex DNA oligonucleotide should inhibit transcription of only one, without interfering in the transcription of the others.

A computational search system has been developed to identify potential triplex DNA forming regions in the three human *CaM* genes. A further function of the system is automatic design of triplex DNA oligonucleotides which will interact specifically with one of the three *CaM* genes, preferentially in the promoter site. That is, the program produces potential DNA oligonucleotide sequences specific to one of the three genes. This search system is based on logic programming techniques such as constraint logic programming and logic grammars [Sear93]. SICStus Prolog, with its various constraint libraries, is the implementation platform. To date our system has shown good results identifying possible triplex DNA forming regions in the three *CaM* genes. Current study involves designing the three groups of triplex DNA oligonucleotides. To conclude the project, prospective DNA sequences will be supplied to a collaborating molecular biology lab where their binding specificity will be determined.

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