# Synthesis of novel peptides through Ugi-ligatio-n and their anti-cancer activities

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Abstract Proline-rich heptapeptide was synthesized and its structure was modified through Ugi-ligation. The desired pseudopeptides were separated as diastereomers and their anti-cancer activities were investigated. Their in vitro anti-cancer activities were investigated by treating HL60 (leukemia cancer cells), MCF7 (breast cancer cells) and A549 (lung cancer cells) cells with appropriate amounts of synthesized peptides. Our in vitro studies suggest that compounds **11a-b**, **11i-j**, and **11e** had little or no effect on cancer cells viabilities.

Key words Ugi-ligation · Ligation of peptides · Anti-cancer activity · Pseudopeptides

## Introduction

The interaction of some regulatory proteins with tran- scriptional regulatory elements with in genome might reg-ulate gene expression. Assays were deployed to systematically identify DNA-binding transcriptional regulators in nuclear extracts (Mirzaei et al. 20I:,). They identified *IS* regulators that bound specifically to distinct regions along −600 bp of the regulatory sequence. More than 100 active regulatory DNAs have been identified in F9 cells correspond to promoter elements, which display several features of endogenous transcriptional regulators, including CpG islands (Yaragatti et al. 2008; Akopov et al. 2007). The availability of complete genome sequence has made it possible to develop computational methods for the detection of transcriptional regulatory elements. The physiological roles of DNA-binding proteins depend upon the precise interactions between amino acids in the DNA-binding protein and nucleotides in the DNA-binding site.

How can we identify features of a DNA-binding site or DNA-binding protein? Many DNA-binding proteins have common structural motifs involved in DNA-protein interactions. But it is not possible to identify the amino acids involved in DNA-binding by simple sequence gazing. Therefore, the critical nucleotides in a DNA-binding site and the interacting amino acids in DNA-binding protein must be determined empirically (Maloy et al. 19%).

Based on DNA-Protein interactions, we have taken specific regions of ras oncogene promoter within the CpG islands in to consideration to design some hypothetical heptapeptides (Scheme I). The proposed mechanism of action, although has not been determined yet, may be due to the direct/or indirect repression of oncogenic activities at transcriptional level. At the extreme, they can also function as "switches", which can turn a gene on and off.

The selected heptapeptide was then chemically modified to enhance its potency as a potential anti-cancer drug. The selected chemical modification was combination of bio- logically active peptide segments. There are several methods for the coupling of peptide segments; among them, native chemical ligation is the most useful method employed. The native chemical ligation (NCL) reaction is a powerful method to join two unprotected peptides in

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