

# Modeling Studies Suggest the Modified Dipeptide Analog Phenylacetyl-amino-2,6-piperidinedione may Interact with DNA

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## Abstract

Molecular modeling technology developed in our laboratories has revealed that the modified dipeptide 3-phenylacetyl-amino-2,6-piperidinedione (A10) fits in a stereo-specific manner between base pairs in double stranded DNA. Given that the mode of action of some carcinogens involves intercalation and covalent binding to DNA, we predicted that A10 might compete with the carcinogens for binding to DNA and thus possess antitumorigenic activity. Experimental evidence now supports these predictions.

Research investigation in our laboratories using a variety of modeling techniques have revealed that a wide range of naturally occurring molecules exhibit stereochemical complementarity with double stranded DNA (Table 1) (1-6). This discovery has been termed the stereochemical logic of gene structure. The stereochemical logic was defined as those unique features of gene structure which ultimately dictate constraints on the structure, function, activity and metabolism of small molecules (3). The logic has led to a technology which can be used to predict biological activity (6). Herein, we describe the application of this technology to a new antitumorigenic compound, A10.

Table 1. Naturally occurring compounds that exhibit stereochemical complementarity with DNA

Amino acids	Prostaglandins
Cyclic nucleotides	Steroid hormones
Insect Hormones	Sugars
Neurotransmitters	Thyroid hormones
Pheromones	Vitamins
Phytohormones	

The modified dipeptide 3-phenylacetyl-amino-2,6-piperidinedione was originally isolated from human urine and termed A10 based upon the chromatographic fraction from which it was isolated. The structure was confirmed by the usual spectroscopic techniques, independent