New Product Highlights

WP900: Highly selective left-handed DNA binding molecule

B-DNA, or right-handed DNA, is the most prevalent form of DNA in the body. Left-handed DNA is known as Z-DNA and was first thought to be an artifact. However, in 1999, Z-DNA was discovered in living cells and could be transformed from B-DNA during gene transcription. Z-DNA is the target of the RNA-editing enzyme, adenosine deaminase, that uses the left-handed DNA as an anchor while it slides along newly transcribed RNA, making small changes that eventually create modified proteins. Although Z-DNA is only present for a short period of time, and only makes up a tiny percentage of total DNA, it may have a very important biological function.

WP900 (Prod. No. W 4013), an anthracycline, is the left-handed enantiomer of the anticancer natural product (+)-daunorubicin (Prod. No. D 8809) [1, 2]. WP900 and (+)-daunorubicin bind selectively to Z-DNA and B-DNA forms, respectively, of synthetic DNA. They both drive the allosteric conversion of DNA to the chiral form preferred by each ligand [3]. WP900 is a weak DNA binder but has the same pKa and lipophilicity as the natural product (+)-daunorubicin [4].

WP900 is an antibiotic shown to have activity against multidrug-resistant cancer cells. It retains cytotoxic activities over a number of multidrug resistant cell variants as compared to (+)-daunorubicin. WP900 is cytotoxic to cancer cells, making it a possible compound for studying Z-DNA-targeted anticancer agents. WP900 may be a potential tool for investigating the significance and function of left-handed DNA in vivo. It may also be used for studying the shifting balance between left- and right-handed forms of DNA, a new approach in drug discovery and control of gene expression.

Anti-Aurora B: chromosomal passenger protein

Aurora B (AIRK2, AIR-2 kinase, AILM-1) is a serine/threonine kinase that plays key roles in chromosome segregation, cytokinesis and cancer development [1, 2]. It also plays a role in chromosomal condensation by phosphorylating histone H3 [3]. In C. elegans, Aurora-B is required for normal localization and function of ZEN-4/CeMKLP, a kinesin-related protein essential for completion of cytokinesis [4]. Loss of the Aurora B kinase results in chromosome segregation defects and failures in cytokinesis [2].

Aurora B is evolutionarily conserved from yeast to human. The Drosophila serine/threonine protein kinase Aurora and the S. cerevisiae Jpl1 kinase are highly homologous to human Aurora B [5]. Aurora B displays a localization pattern typical of chromosomal passenger protein, such as the inner centromeric proteins, INCENP, TD-60 and Survivin [1]. INCENP and Survivin interact directly with Aurora B [6]. Chromosomal passenger proteins undergo dynamic redistribution during mitosis. They localize at centromeres during prometaphase, and relocate to midzone microtubules and midbodies during anaphase and telophase [7]. The mRNA and protein levels of Aurora B are induced during G2M and decrease rapidly after the end of mitosis [2]. Levels of Aurora B are increased in several human cancer cell lines [8].

Sigma-RBI is pleased to introduce Anti-Aurora B (Prod. No. A 5102) that was developed using a synthetic peptide corresponding to amino acid residues 1-19 of human Aurora B. Anti-Aurora B recognizes human, mouse, and rat Aurora B. Applications include immunoblotting (41 kDa), immunoprecipitation, and immunofluorescence. Detection of the Aurora B band by immunoblotting is specific for the immunizing peptide.

References