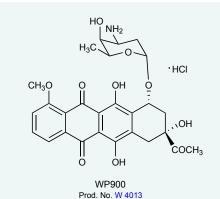
New Product Highlights

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. <u>W 4013</u>), an anthracycline, is the lefthanded enantiomer of the anticancer natural product (+)-dauborubicin (Prod. No. <u>D 8809</u>) [1,2]. WP900 and (+)-dauborubicin 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.



References

- 1. Borman, S., Chem. & Eng. News, 78, 7-8 (2000).
- 2. Waring, M., Proc. Natl. Acad. Sci. USA, 97, 11685-11687 (2000).
- 3. Qu, X., et al., Proc. Natl. Acad. Sci. USA, 97, 12032-12037 (2000).
- Loetchutinat, C., et al., Eur. J. Biochem., 268, 4459-4467 (2001).
- Loetchutinat, C., et al., Biochem. Pharmacol., 62, 561-567 (2001).

Anti-Aurora B: chromosomal passenger protein

Aurora B (AIRK2, AIR-2 kinase, AIM-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 cyto-kinesis [4]. Loss of the Aurora B kinase results in chromosome segregation defects and failures in cytokinesis [2].

Aurora B is evolutionally conserved from yeast to human. The *Drosophila* serine/threonine protein kinase Aurora and the *S. cerevisiae* lpl1 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 centromers 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. <u>A 5102</u>) 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 specifically inhibited with the immunizing peptide.

References

- 1. Adams, R.R., et al., Trends Cell Biol., 11, 49-54 (2001).
- 2. Terada, Y., et al., EMBO J., 17, 667-676 (1998)
- 3. Hsu, J.Y., et al., Cell, **102**, 279-291 (2000).
- 4. Severson, A.F., et al., Curr. Biol., 10, 1162-1171 (2000).
- 5. Giet, R., and Prigent, C., J. Cell Sci., 112, 3591-3601 (1999).
- 6. Bolton, M.A., et al., Mol. Biol. Cell, 13, 3064-3077 (2002).
- 7. Murata-Hori, M., et al., Mol. Biol. Cell, 13, 1099-1108 (2002).
- 8. Adams, R.R., et al., Chromosoma, 110, 65-74 (2001).