



Human BUB Genes: Mitotic Checkpoint Kinases

Dr. Tim Yen and colleagues of Fox Chase Cancer Center have discovered and characterized human BUB genes that play an important role in the mitotic checkpoint.

Background: The BUB family of serine/threonine kinases is a major target of oncology therapeutic research and developmentⁱ. hBUB1 and hBUBR1 are kinases that associate with hBUB3 and are essential components of the mitotic checkpoint. hBUBR1 appears to provide two checkpoint functions by monitoring CENP-E-dependent activities at the kinetochore and by regulating cyclosome/APC activity.

hBUBR1 is required in order for microtubule inhibitors to arrest cells in mitosisⁱⁱ. Non-mutational inactivation of hBUB1 and hBUBR1 appear related to stage of colon cancerⁱⁱⁱ and could be related to aneuploidy in human colorectal and other cancers.

Applications:

- o **Research:** This technology is useful for research on mitotic checkpoint mechanisms and for screening. **BUB cDNA and oligonucleotides are commonly included as components of microarrays.**
- o **Cancer Drug Discovery:** Small molecules able to disrupt regulation or function of BUB proteins have the **potential to enhance the effects of anti-tubulin drugsⁱ** by forcing proliferating cells through mitosis in the absence of a functional mitotic spindle, resulting in damage and cell death.
- o **A pharmaceutical compound that inhibits Aurora A and Aurora B kinases has been reported to inhibit BUBR1 phosphorylation^{iv}.**

Opportunity: Commercial and research use licenses to intellectual property are available. Monoclonal antibodies against hBUB and hBUBr1 are also available for licensing.

Patent status: Human BUB genes are covered by U.S. Patent 6,593,098.

ⁱ Wood, KW et al. 2001. Curr. Opinion in Pharmacology 1:370-377.

ⁱⁱ Chan, GK et al. 1999. J. Cell Biol. 146: 941-954.

ⁱⁱⁱ Shichiri M et al. 2002. Cancer Research 62: 13-17.

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About Fox Chase Cancer Center

Fox Chase Cancer Center is an independent, not-for-profit institution devoted to cancer treatment and prevention; clinical research, and basic research on cancer prevention, initiation, and progression. More than 150 clinical trials are typically ongoing at any time. Key discoveries of Fox Chase researchers include the Scid mouse and the Hepatitis B vaccine. Fox Chase was one of the first institutes to be designated as a comprehensive cancer center by the National Cancer Institute and remains among the top three NCI-core grant recipients in the country. Fox Chase is a founding member of the National Comprehensive Cancer Network, an alliance of the world's leading cancer centers, and has a network of hospital affiliations in Pennsylvania, New Jersey and Delaware.