BET Proteins and Gene Expression

BET Proteins and Cancer

Inhibiting BET Proteins

BET Proteins

BET proteins are a group of “reader” proteins (BRD2, BRD3, BRD4 and BRDT) that recognize chemical marks placed in DNA by “writer” and “eraser” proteins. • “Writers” and “erasers” add and remove chemical marks, respectively.1,2

BET proteins bind to these chemical marks triggering the activation of transcription of certain genes.1,2

Transcription is the process by which information in DNA is copied into RNA, which can then code for and produce proteins.

BET proteins are found on various normal cell types and are responsible for regulating a variety of cellular processes.1,2

Inhibiting BET proteins may downregulate (suppress) the transcription of cancer promoting genes, resulting in inhibition of cancer growth.2

BET inhibition has led to a reduction in malignant cell growth in preclinical models.2 BET inhibition:

• Has decreased cell growth and increased cell death in multiple cancer cell lines.3
• Can be leveraged in combination with other types of cancer treatment.4
• In combination with immune checkpoint blockade may enhance anti-cancer activity more than either mechanism alone.5,6
• May help to restore patient sensitivity to other important cancer treatments, like chemotherapies, hormone therapies or other pathway inhibitors.7,8

One approach is to inhibit BET proteins using oral small molecules, some of which can cross the blood brain barrier (BBB).

• This may allow the treatment of brain cancers including glioblastoma, an aggressive type of brain cancer.

Cancer cells can take advantage of the modulation effect of BET proteins by using them to upregulate (or amplify) expression of cancer promoting genes, thereby aiding tumor growth.2

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Bristol Myers Squibb is committed to identifying new treatments for patients in need and is evaluating the effects of BET inhibition in the clinic in blood cancers and in solid tumors.