

BRD4 is a target for treating epileptic seizures

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Technology Summary

BRD4 is a member of the the **B**romodomain and **E**xtra**T**erminal (BET) domain family of proteins which are responsible for “reading” acetylated lysine residues and regulating transcription in a variety of cell types in response to external signals. Aberrant BRD4/BET activity has been linked to a certain types of cancers which resulted in the development of a number of small molecule inhibitors, such as Jq1, that are currently being tested in clinical trials. However, very little is known about BRD4 activity in the brain.

Studies carried out by Rockefeller University investigators Drs. Erica Korb, C. David Allis, and Robert B. Darnell showed that Jq1 caused changes in normal mouse neuronal cells by decreasing BRD4 activity, linking it to transcriptional processes important for learning and memory formation. To investigate whether BRD4 plays a role in neurological disorders, Dr. Korb and colleagues tested the Jq1 in a mouse model of chemically induced seizures – a condition caused by over-activity of the brain. The mice treated with the BRD4 inhibitor had a lower rate of seizures and mortality than mice that had not been treated with the drug. Ongoing research indicates that Brd4 inhibition also may be beneficial in other neurodevelopmental disorders that stem from similar causes. Overall these findings show significant promise for developing compounds specifically targeting BRD4 to help further probe the role of BRD4 in neurological diseases, and to develop novel therapeutics.

Advantage

Targeting BRD4 in neurodegenerative diseases is novel and underexplored

Area of Application:

Seizure susceptibility and memory formation

Stage of Development:

In vivo animal studies

Lead Inventor:

Dr. David Allis, Dr. Erica Korb, and Dr. Robert Darnell

Patent Information:

U.S. provisional patent application pending

Reference:

Korb et al, BET protein BRD4 activates transcription in neurons and BET inhibitor Jq1 blocks memory in mice, *Nature Neuroscience*, **18**, 1464–1473 (2015).

<http://www.nature.com/neuro/journal/v18/n10/abs/nn.4095.html>