

# Identification of specific inhibitors of MutS and MutL homolog function

This invention includes 1) methods for testing an agent for the ability to inhibit MutS $\beta$ , by forming an assay that includes the agent, MutL $\alpha$  and MutS $\beta$ , and evaluating interaction between MutL $\alpha$  and MutS $\beta$  in the assay and 2) a means for and testing the agent for the ability to inhibit the interaction between MutL $\alpha$  and MutS $\alpha$  by forming an assay including the agent, MutL $\alpha$  and MutS $\alpha$ , and evaluating interaction between MutL $\alpha$  and MutS $\alpha$  in the assay.

These methods will allow the identification of agents having the ability to specifically inhibit the interaction between MutL $\alpha$  and MutS $\beta$ . Identification of these agents may be used to develop structurally related agents that can then be tested by the methods of the invention for the ability to specifically inhibit the interaction between MutL $\alpha$  and MutS $\beta$ . It is envisioned that agents having the ability to specifically inhibit the interaction between MutL $\alpha$  and MutS $\beta$  could be useful in treating individuals having or at risk for developing deleterious conditions associated with MutS $\beta$  activity, e.g., neurological disorders caused by the expansion of (CAG)<sub>n</sub> repeats.

The methods of the invention will also allow the identification of agents having the ability to specifically inhibit the interaction between MutL $\alpha$ , and MutS $\alpha$ . Such agents may be useful as research tools in further studies of interactions of proteins involved in mismatch repair.

This invention also provides a kit for screening agents for the ability to inhibit the interaction between MutL $\alpha$  and MutS $\alpha$  or MutS $\beta$  that includes MutL $\alpha$ , MutS $\alpha$  and/or MutS $\beta$ , and a linear heteroduplex DNA substrate or a linear homoduplex DNA control attached to a solid support through one end of the substrate or control. Suitable DNA substrates contain a MutS $\alpha$ - or MutS $\beta$ -recognizable mismatch.

## Patents

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Title: METHODS AND COMPOSITIONS FOR IDENTIFYING INHIBITORS OF MUTS-ALPHA OR MUTS-BETA INTERACTION WITH MUTL-ALPHA

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# Duke

## LICENSING & VENTURES

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