

Compositions and Methods for Identifying Agents that Alter Expression of Survivin

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Summary:

Provided are compositions and methods for identifying agents that can modulate expression of the human survivin gene. The compositions include eukaryotic cells that contain a human survivin promoter sequence operably linked to a reporter gene. The method comprises determining whether a test agent can modulate transcription from a human survivin promoter sequence by adding a test agent to eukaryotic containing a human survivin promoter sequence operably linked to a reporter gene, measuring expression of the reporter gene and comparing expression of the reporter gene from to a control, wherein an increase or decrease of expression of the reporter gene relative to the control is indicative that the test agent can modulate transcription from a human survivin promoter. The method also comprises the use of SPlucTg mice for preclinical drug identification, including testing of candidate drug toxicity and efficacy.

Detail:

The present invention provides eukaryotic cells comprising a human survivin promoter polynucleotide sequence operably linked to a reporter gene. The cells are useful for identifying agents that can modulate survivin gene transcription. In one embodiment, the cells are stably transfected cancer cells lines. In another embodiment, the invention provides a transgenic mouse comprising a germ line insertion of the survivin promoter in operable linkage with the reporter gene. Also provided are methods for identifying agents that can modulate survivin expression. The method comprises adding a test agent to cells comprising a human survivin promoter in operable linkage with a reporter gene. By comparison with a control, agents that can either increase or decrease transcription from the survivin promoter, as evidenced by increased or decreased expression of the reporter gene, can be identified. Thus, the invention is suitable for identifying agents that are expected to have therapeutic benefit for cancer patients, as well as for other disorders wherein it would be desirable to modulate the expression of survivin.