

A new validated HTS to identify new first-in-class antitumoral compounds

BACKGROUND

RB was the first described tumor-suppressor protein and its inactivation is known to trigger a large variety of tumors. More than 80% of human cancer carries mutations on the RB/CDK/INK pathway, which controls cell cycle progression. Loss of RB is seldom involved in the initiation or progression of most human tumors. RB is cyclically inactivated during cell division by CDKs. The N-terminal phosphorylation of RB by p38 bypasses its inactivation by CDKs and prevents proliferation in cancer cells. The discovery of this novel regulatory mechanism allows us to explore and characterize antitumoral compounds, avoiding toxicity and specificity caveats of CDK inhibitors.

THE TECHNOLOGY

Stress-activated protein kinases, as p38, play a key role in controlling different cell-cycle checkpoints. RB phosphorylation by p38 caused an increase of RB affinity to E2F transcription factors, which in turn leads to cyclin expression down-regulation and reduction of cell proliferation. The N-terminal phosphorylation of RB by p38 bypasses its inactivation by CDKs and prevents proliferation in cancer cells. We have developed and validate a HTS system to identify small compounds capable of mimicking the N-term RB phosphorylation for therapeutic applications as new anticancer compounds.

ADVANTAGES

- Rapid and validated method.
- The new molecules will bypass the high CDK activity in the tumor cells.
- As acting so downstream, directly on RB, molecules will be specific enough to avoid undesirable side effects compared with other upstream acting drugs.

STATE OF DEVELOPMENT

Fully developed HTS system. Identification of the first Hits. In process, hit optimization.

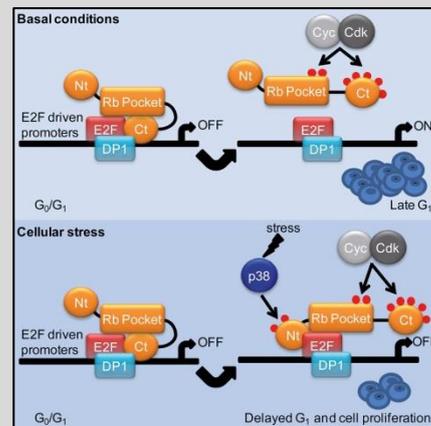
INTELLECTUAL PROPERTY

A priority EP application has been filled in April 2016, and an international PCT application in 2017.

MARKET OPPORTUNITY

The world cancer-treating drugs market reached \$102 billion in 2016 and expected to grow at a compound annual growth rate of approximately 7% in 2020. Oncology continues to be forecasted as leading therapeutic area for developed countries.

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COMMERCIAL OPPORTUNITY

Co-development of new drugs and/or licensing of the technology.

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KEYWORDS

HTS, anticancer drugs, RB phosphorylation

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