Recombinantly produced p27 for use in screening inhibitors of Cdk4/6;Cyc6/p27 kinase complex

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BACKGROUND

Cyclin Dependent Kinases (Cdk) 4 and 6 promote cell proliferation through their kinase activity. The active cellular form of the Cdk 4 or 6 enzyme forms a complex with both cyclin D (CycD) and p27 in vivo. Current therapeutics that target Cdk4 or 6 were generated in a complex that lacked p27 because of difficulties in expressing a recombinant form of p27. This technology describes a recombinantly produced engineered form of p27 that forms stable complexes with Cdk4/6 and CycD in vitro.

TECHNOLOGY DESCRIPTION

The technology encompasses a p27 polypeptide that has an amino acid substitution mutation at one or more of Y74, Y88, or Y89. Exemplary mutations are Y74E, Y74D, Y74R, Y88E, Y88D, Y89E, or Y89D. These mutant p27 polypeptides have been shown to be expressed in E. coli and form active Cdk4/CycD/p27 Cdk6/CycD/p27 kinase complexes in vitro.

APPLICATIONS

Screening for inhibitors of Cdk4/6 trimeric complexes

ADVANTAGES

First ever active in vitro expressed Cdk4/CycD/p27 and Cdk6/CycD/p27 complex

RELATED MATERIALS

- Guiley KZ et al, p27 allosterically activates cyclin-dependent kinase 4 and antagonizes palbociclib inhibition; Science 366, 6571 (2019) - 12/13/2019

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OTHER INFORMATION

KEYWORDS

Cyclin Dependent Kinase Inibitors, Pharmaceutical screening assays, Cancer Drug Targets, Cancer Drug Development

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Research Tools

RELATED CASES

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