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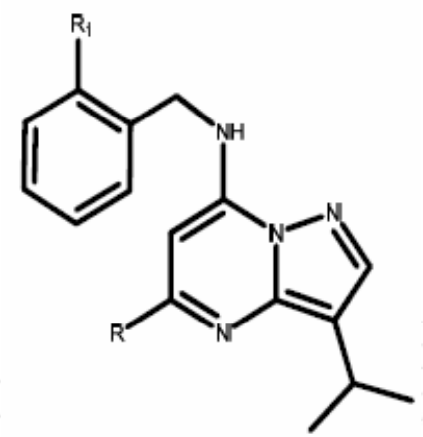
# Cyclin-Dependent Kinase Inhibitors as Cancer Therapeutics




Panya Taysavang
Licensing Associate

Emory OTT Breakfast Club
May 25th, 2010

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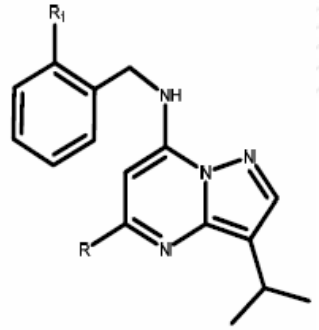
# Opportunity

- Novel, highly selective cyclin-dependent kinase (CDK) inhibitors
- CDKs belong to a group of protein kinases that are involved in a variety of cellular processes
- CDK7 an attractive  target for drug development
- Pyrazolo[1,5-*a*]pyrimidine compounds that are useful for the selective inhibition of CDK7



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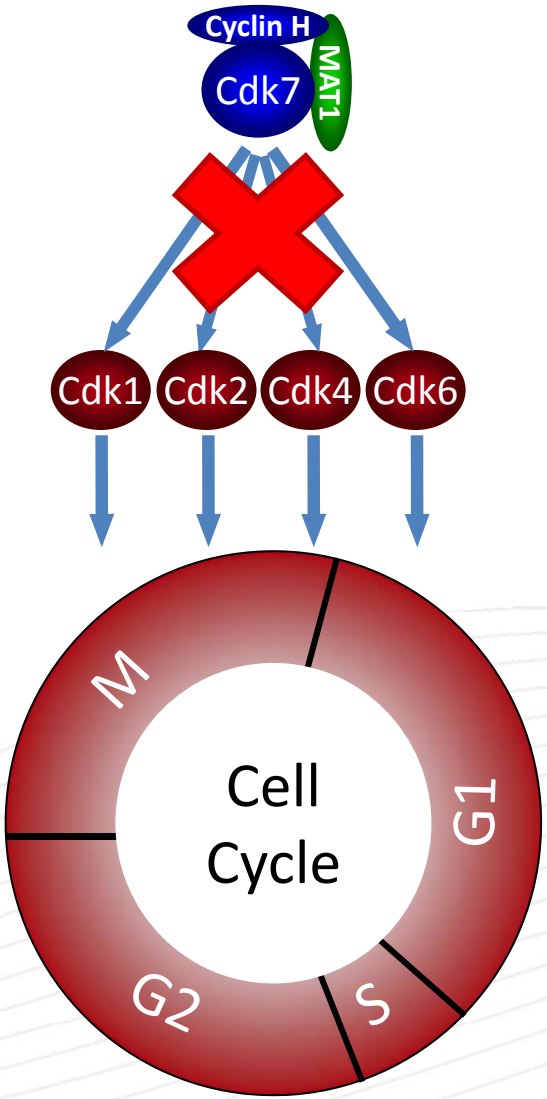
# CDK7 Regulates Cell Cycle Progression




<u>Cell Proliferation</u>

- Cancer
- Inflammation
- Atherosclerosis
- Immune diseases

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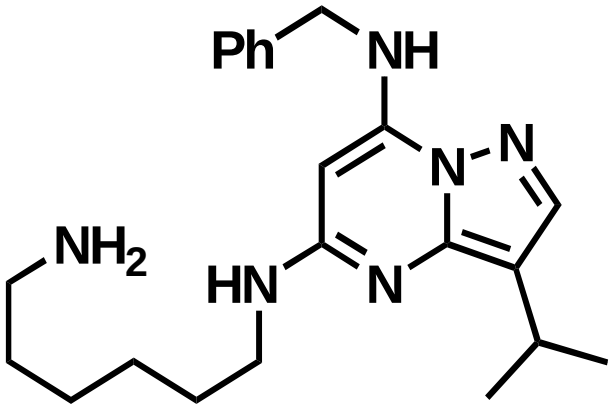
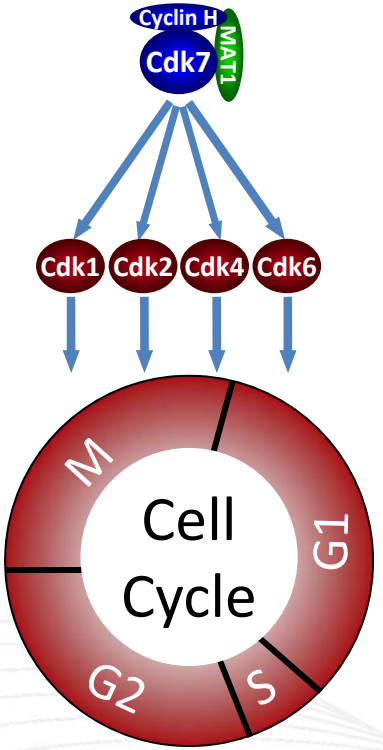
# CDK7 Selectivity of BS-181




**BS-181**




| Kinase | Roscovitine $IC_{50}$ (µM) | BS-181 $IC_{50}$ (µM) |
|---|---|---|
| CDK7 | 0.51 | 0.021 |
| CDK2 | 0.1 | 0.88 |
| CDK1 | 1.8 | 8.1 |
| CDK4 | 15.3 | 33 |
| CDK6 | 28 | 47 |

| Kinase | BS-181 $IC_{50}$ (µM) | **Comparative CDK7 Selectivity** |
|---|---|---|
| CDK7 | 0.021 | -- |
| CDK2 | 0.88 | 42X |
| CDK1 | 8.1 | 386X |
| CDK4 | 33 | 1571X |
| CDK6 | 47 | 2238X |

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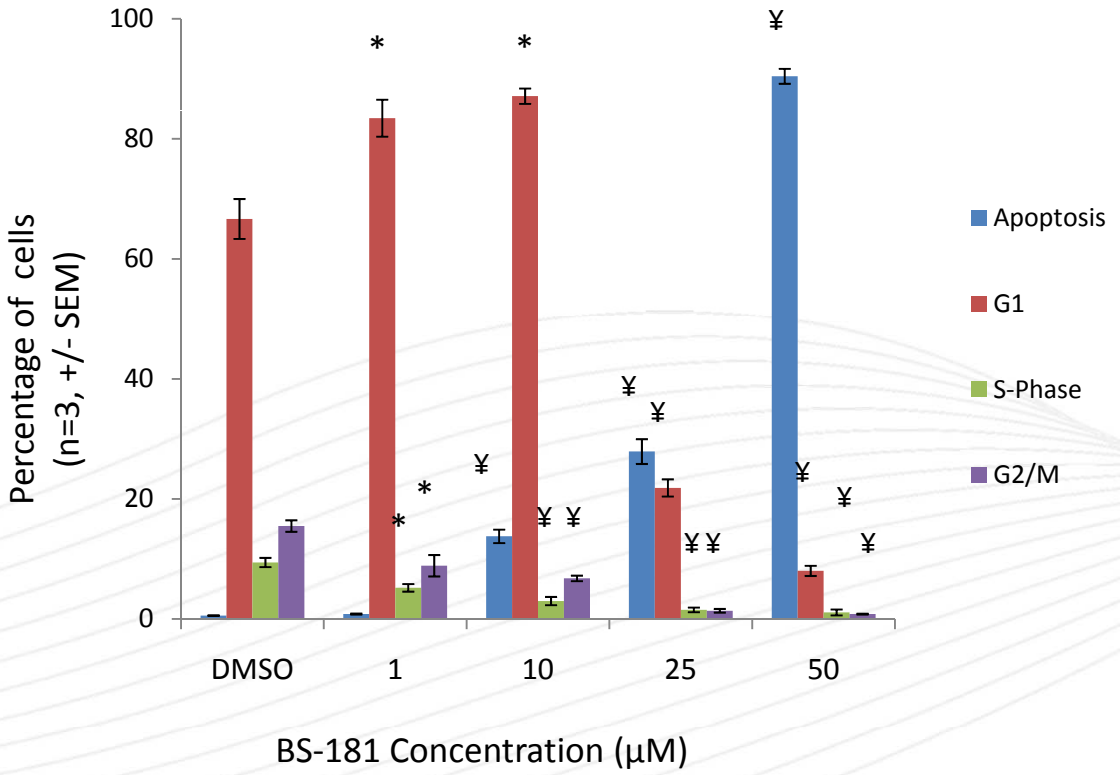
# BS-181 Inhibits Cell Growth and Promotes Apoptosis



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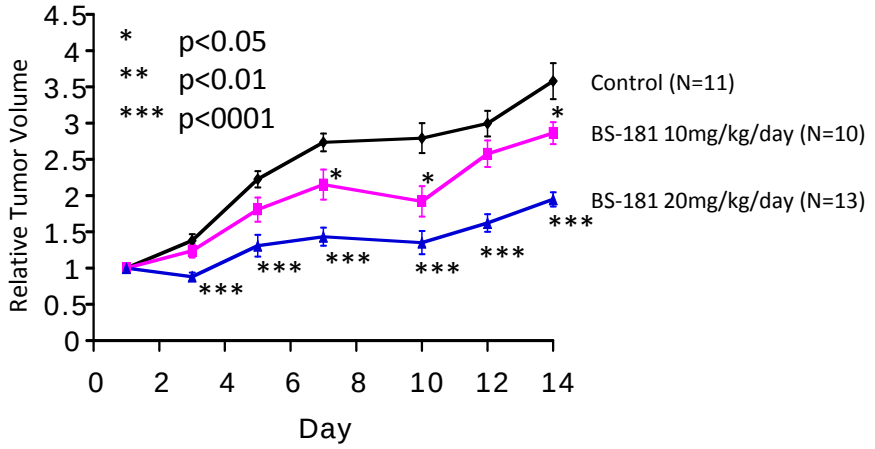
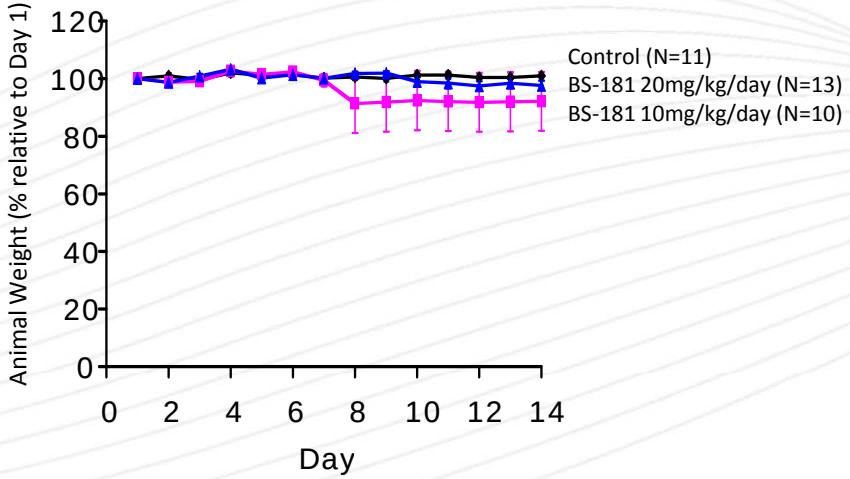
# BS-181 Inhibits Growth of MCF-7 Tumors in Nude Mice



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# BS-181 PK

| Route of Administration | Dose | Bioavailability | T1/2 |
|---|---|---|---|
| IP | 10mg/kg | 37% | 6.75hrs |

| Route of Administration | Dose | Bioavailability | T1/2 |
|---|---|---|---|
| Oral | 10mg/kg | 2% | 1.15hrs |

| Route of Administration | Dose | Bioavailability | T1/2 |
|---|---|---|---|
| IV | 10mg/kg | - | 5.72hrs |

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# Intellectual Property

- National stage applications pending
  - US, EPO, AU, and CA
  - July 2008 filing
- Claims address:
  - Novel compositions
  - Synthesis method
  - Methods of treatment

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# Summary and R&D Status

- CDK7 selective compound
- Refinements of BS-181 structure underway to increase bioavailability
- Cancer Research UK grant
  - £3m funding
  - Compound development
  - Clinical studies (Phase I trial)