Design and Synthesis of a Heterocyclic Compound Collection for Probing the Spatial Characteristics of ATP Binding Sites

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CSIR Biosciences

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• The kinases
• The nature of the ATP site
• A basis for selectivity
• Types of potential guest molecules
• Methodology for preparation
The Kinases

- Proteins which transfer phosphoryl residues
- Utilise ATP as phosphate source
- All have an ATP site
- Why are kinases attractive targets?
Basic Structural Characteristics of the ATP Site

Typical ATP binding site

Adenine Binding Region

Sugar Binding Region

Hydrophobic Region
Pharmaceutical example: Interactions of SB203580 in the p38 MAP Kinase
Rational Basis of Design
Scaffold Selection

Pyrimidines

Purines

Imidazopyridines
Spatial Comparison of Scaffolds
Pyrimidines and Purines

\[
\text{Pyrimidines: } \quad \text{Purines: }
\]

1. Pyrimidines: 
   - [Diagram of pyrimidine structure]
2. Purines: 
   - [Diagram of purine structure]
Synthesis of Pyrimidines and Purines

Slide 10

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Imidazopyridines
The Classical Approach

\[
\text{NH}_2 \text{N} + \text{O} \text{O} \text{Cl} \rightarrow \text{N} \text{N} \text{Cl}
\]
Diversity Orientated Approach

\[
\text{NH}_2 \quad \overset{\text{RCHO}}{\longrightarrow} \quad \text{N} \quad \overset{\text{R}}{\longrightarrow} \quad \text{NH}
\]

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<table>
<thead>
<tr>
<th>Aldehyde</th>
<th>Isocyanide</th>
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<td><strong>PhCHO</strong></td>
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<tr>
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The Way Ahead

Explore the untapped dimension
Kinase and ATP –ase studies
Thanks To

CSIR Thematic Programmes

Department of Science and Technology