



*Peptides & Peptide Mimetics Technology*

# *Peptide Mimetics Technology*

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## **Peptide**

- + Easy lead for biology
  - Poor drug properties
  - Not stable
  - Low bioavailability
- => Needs optimization for  
1<sup>st</sup> generation drug candidate?

## **Mimetic**

- + Takes advantage of peptide data
  - + Drug-like properties
  - + Stable
  - + Bioavailable
- = Drug Candidate

# *Peptide Optimization for 1st Generation*

*Proof-of-concept or defined clinical target*

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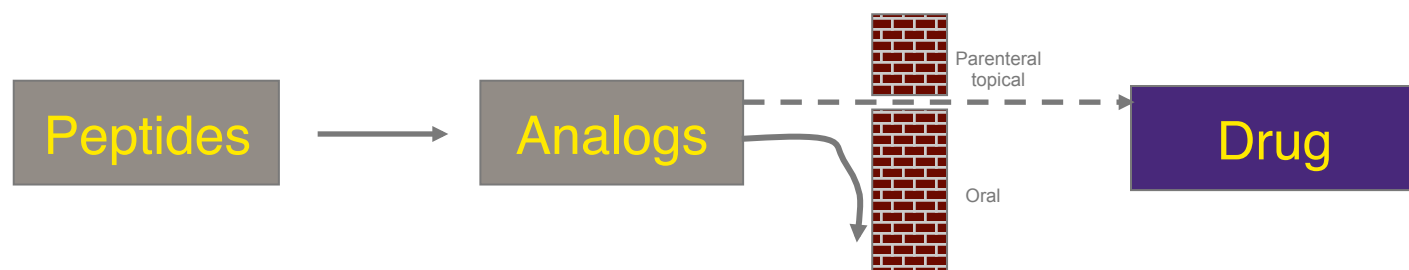
- Define minimally active sequence
- Develop peptide SAR and pharmacophore
  - Side chain variants (natural, unnatural)
  - Backbone recognition (N-Me, cyclic, and amide variants)
  - Use available biostructural data (pharmacophore)
  - Add conformational constraints
  - N- and C-caps
- Stabilize, enhance transport, optimize PK/ADME

==> Peptide analog as drug for some indications

==> Lead for mimetics

# Provid Peptide Mimetics Approach

## Traditional approach



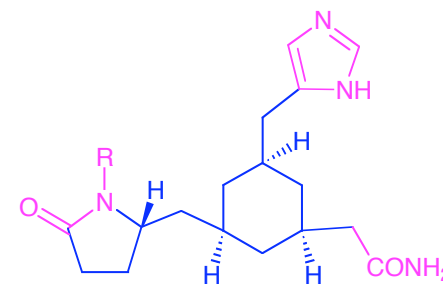
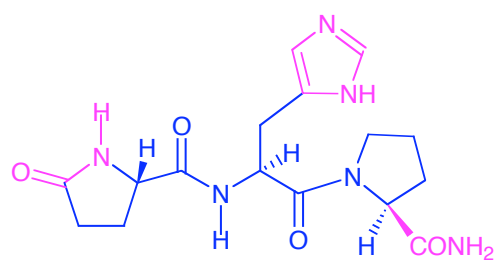
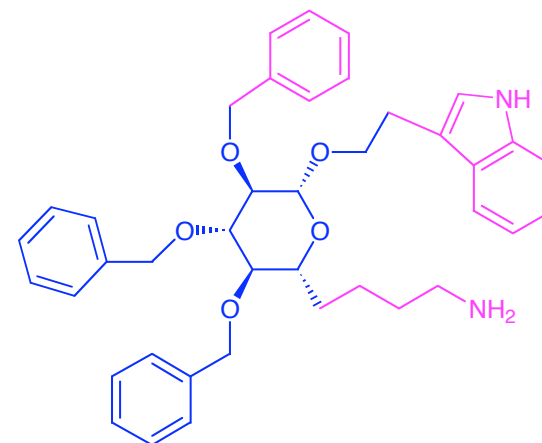
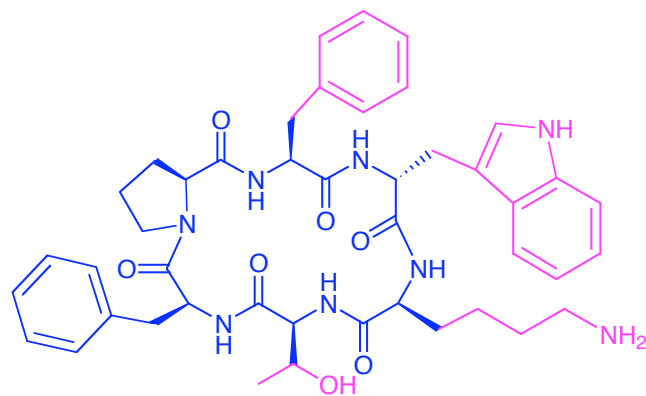
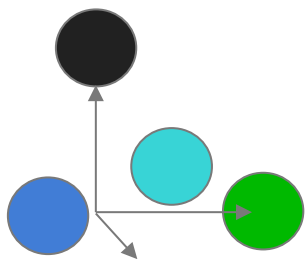
## Provid approach



Peptide mimetics incorporate the biologically important features of a peptide on a small molecule, drug-like scaffold.

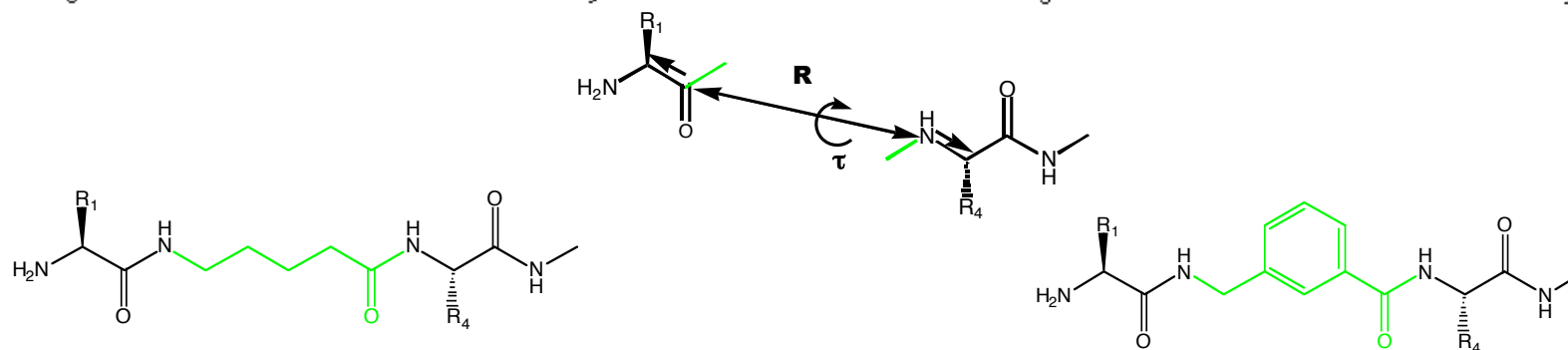
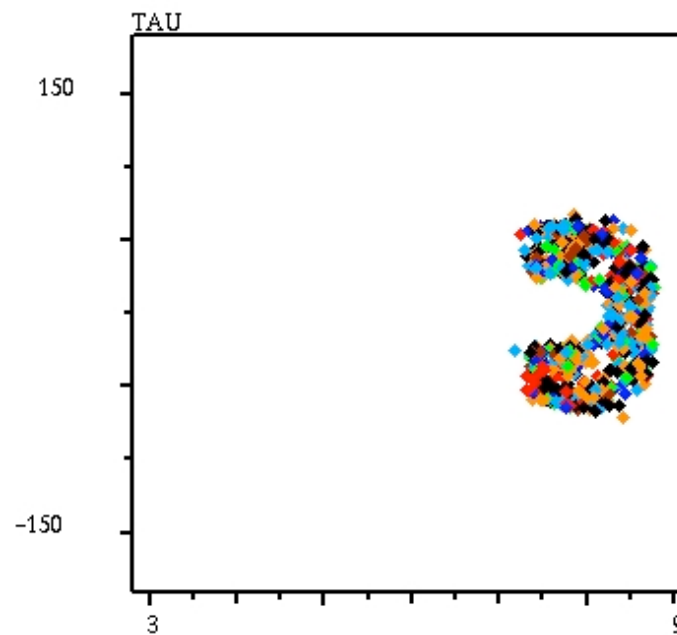
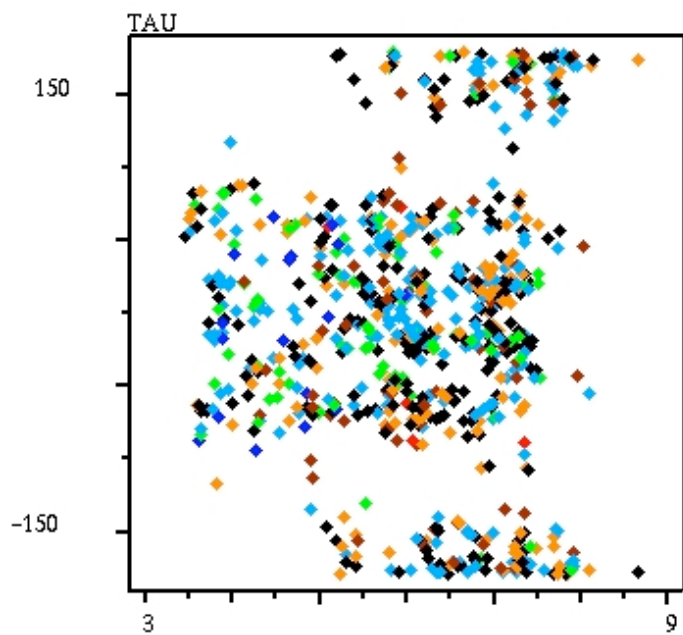
# Peptide Mimetics—Backbone Replacement

3-Dimensional presentation



Hirschmann, Smith (U. Penn)  
Olson (Roche)

# Constraints in Peptide Mimetics



## *Strategy: Peptide Mimetics*

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- Develop non-peptide structures that present the binding epitope in the context of a small molecule
  - Design multiple scaffolds and chemotypes to explore “presentation” of pharmacophore in 3D space
  - Use peptide SAR (side chains and backbone)
  - Concurrent with peptide lead SAR and optimization
- *Goal: Identify active mimetic series suitable for optimization as a small molecule peptide mimetic.*

## *Mimetics Optimization*

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- Optimization through cycles of pharmacophoric group manipulation on best scaffolds
  - Optimization based on in vivo efficacy, transport/bioavailability, and PK, ADMET characteristics.
  - Assessment of and chemical modifications to achieve high target specificity and to avoid off target side effects
- Selection of development candidate and backup/2nd generation compounds
- Support exemplification for patents.
- Develop prototype process suitable for IND candidate
- *Goal: Small molecule drug candidate suitable for IND*

## *Provid Client Peptide Mimetic Projects*

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- Sequenom: Isoform-specific disruptors of PKA localization (PKA-AKAP interaction)
- Duke: Inhibitors of polyglutamine aggregation for Huntington's disease
- Pohan U: Inhibitors of APP cleavage by BACE-1 for Alzheimer's disease
- Cognosci: APO-E mimetics
- Palatin: Peptide mimetics for MCR
- BTG: CD23 ligands
- Rutgers: RNA polymerase inhibitors
- Provid: HLA-DQ2 inhibitors for celiac disease