

Medicilon Peptide & Macrocyclic Peptide Drug Discovery Service Platform

Peptides as a therapeutic method attract much attention due to the synthetic accessibility, high degree of specific binding, and the ability to target protein surfaces traditionally considered "undruggable". Macrocyclic peptides possess a lot of pharmacological characteristics distinct from other well-established therapeutic molecular classes, resulting in a versatile drug modality with a unique profile of advantages.

Peptide Drug Advantages

- Synthetic accessibility
- Low immunogenicity and toxicity
- High binding affinity and selectivity
- The ability to target protein surfaces traditionally considered "undruggable"
- Macrocyclic peptide: Compared to the linear peptide precursor
 - more stable
 - more selective
 - more potent
 - increased membrane permeability
- Advances in high-throughput in vitro screening techniques
 - Phage display
 - mRNA display
 - Flexizymetechnology

Medicilon Peptide Drug Discovery Service

♥ Full Time Equivalent (FTE)

- Dedicated R&D and Management team: standard 10 FTE team: 1 senior group leader (8-10 years) + 1 senior chemist + 2 subgroup leader (3-7 years), senior scientist, middle level scientist, junior scientist (3 member subgroup)
- Flexibility in
 - Project priorities
 - Staffing
 - Protocol

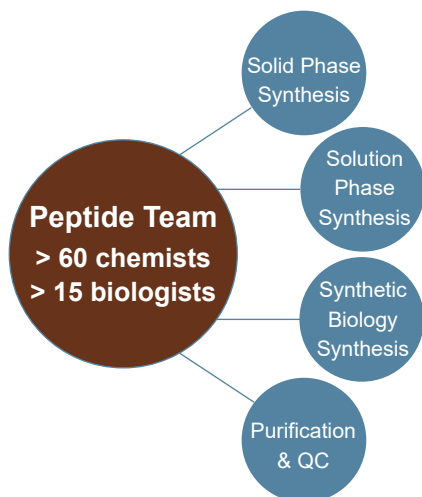
♥ Fee For Service (FFS)

- Services provided for specific needs/projects. Fixed fees and delivery timeframe.
 - Customization of needs
 - mg to kg custom synthesis
 - chiral separation
 - impurity separation
- CMC work for IND application and IND investigation
- Non-GMP and GMP scale-up, commercial production of API and intermediates

♥ Others

- Customized synthesis: mg-100 g scale
 - Linear peptides (up to 50 AAs via one-by one coupling; >70 AAs via ligation strategy)
 - Cyclic peptides (S-S bridge, lactam/lactone, thioether, olefin metathesis, click reaction etc.)
 - Modified peptides (pegylation, DOTA, phosphorylation, thiopeptide etc.)
 - Peptidomimetics
 - Peptides containing special amino acid: containing isotope atom amino acid, D-amino-acid, other unnatural amino acid etc.
- Macro cyclic peptide library synthesis
- Unnatural AAs Synthesis –Chemical and Enzymatic
- ADC-like compounds
- Saltexchange: TFA/HCl, TFA/acetate

Medicilon Peptide Drug Discovery Service Team



- Solid phase synthesis on resin by Fmoc or other chemistry
- Support various modifications on peptides
- Synthesis by both auto-synthesizer and manual apparatus
- Unnatural amino acid synthesis
- Solution/solid combination synthesis for special peptides
- ADC-like compound synthesis
- mRNA Display technology for coded macro cyclic peptide library synthesis
- Enzymatic catalysis for unnatural amino acid synthesis
- Enzymatic peptide ligation and cyclization
- Various prep-HPLC equipped with up to 20 cm columns
- Multiple types of columns: C18, C8, C4....
- Up to 60L tray-lyophilizer

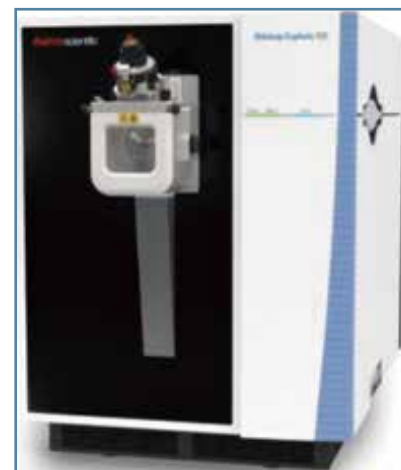
Instruments for Peptide Synthesis & Purification



Customized manual peptide synthesis system



CsBioauto-synthesizer



HRMS



OEB4 lab for ADC project



Automated small scale purification system

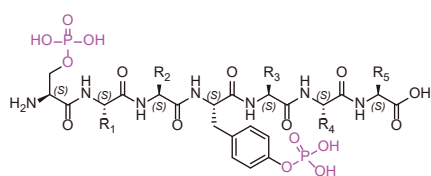
- >60 Chemists
- >40% MS/Ph.D.

- Customized synthesis
- mg to 100 g scale

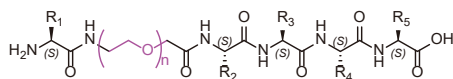
- Unnatural AA
- ADC-like compounds

Peptide Synthesis

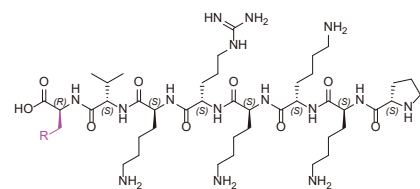
Linear/Modified Peptides



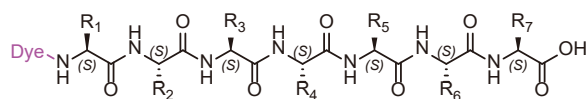
Phospho-peptide



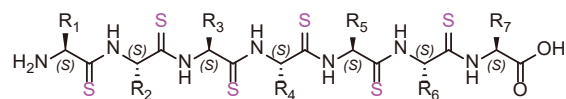
PEGylated peptide



R = SH or aliphatic amine, or other groups used for modification



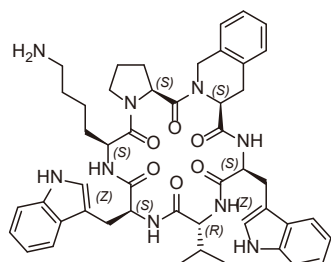
Dye modified peptide



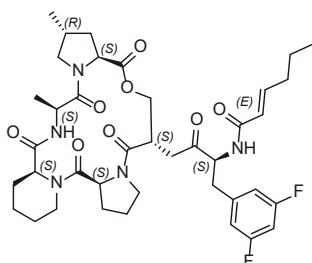
Thio-peptide

- Linear/Modified Peptide synthesis in solution phase, on solid phase and automatic synthesizer
- Peptide modification (N-terminal or side chain modification, C-terminal modification, peptide phosphorylation labeling, methylation and other alkylation modification, isotope labeling, fluorescence modification, PEG modification, peptide protein coupling, etc.)

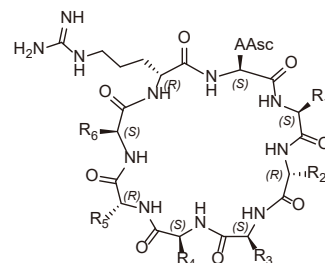
Cyclic Peptides



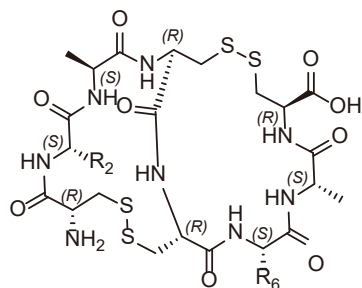
Fixed peptidomimetics
WO2008092281



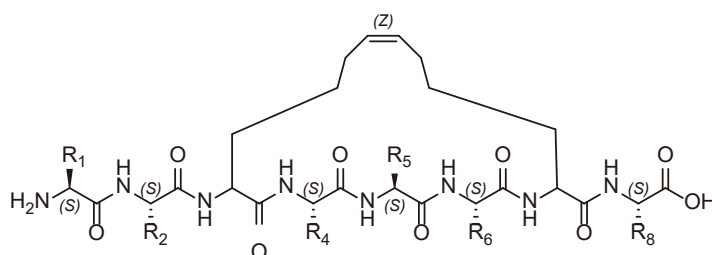
ADEP4
J. Med. Chem.2006, 689



CPPs
WO2022/241408



Bicyclic disulfide bridge

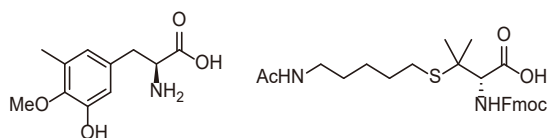
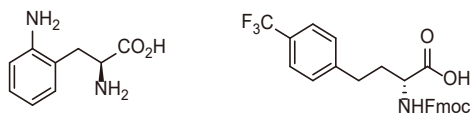
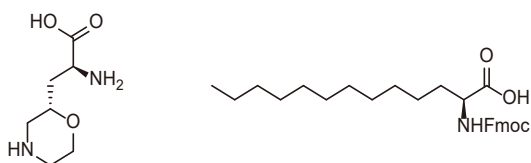


RCM monocyclic peptide

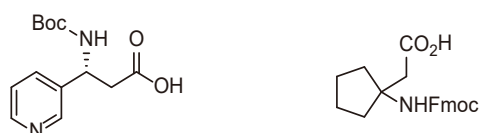
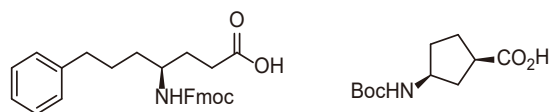
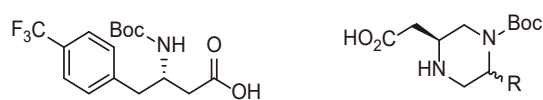
- Cyclic peptides (S-S bridge, lactam/lactone, thioether, olefin metathesis, click reaction etc.)

Unnatural Amino Acids

Enantioselective chemical synthesis



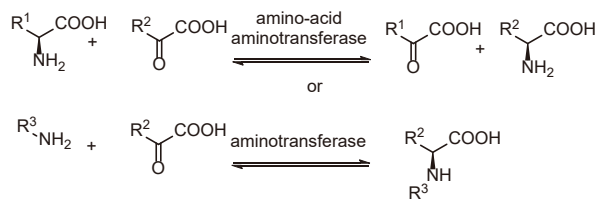
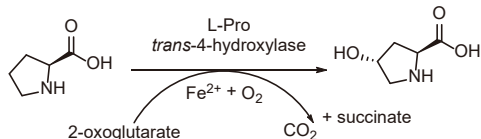
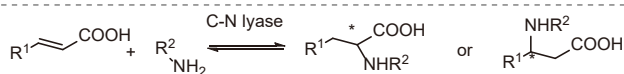
Unnatural α -amino acids



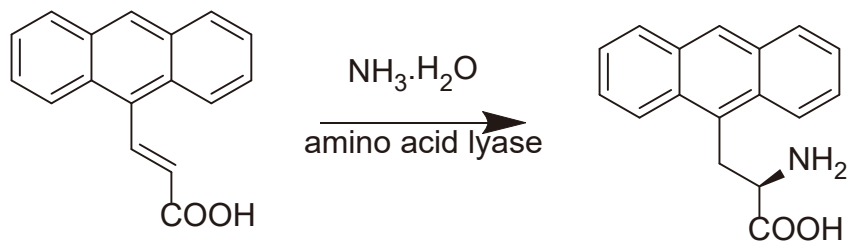
Unnatural β/γ -amino acids

- Rich experience to prepare various unnatural amino acids in-house
- Help client to build up amino acids library
- Explore the synthesis of special AAs upon request

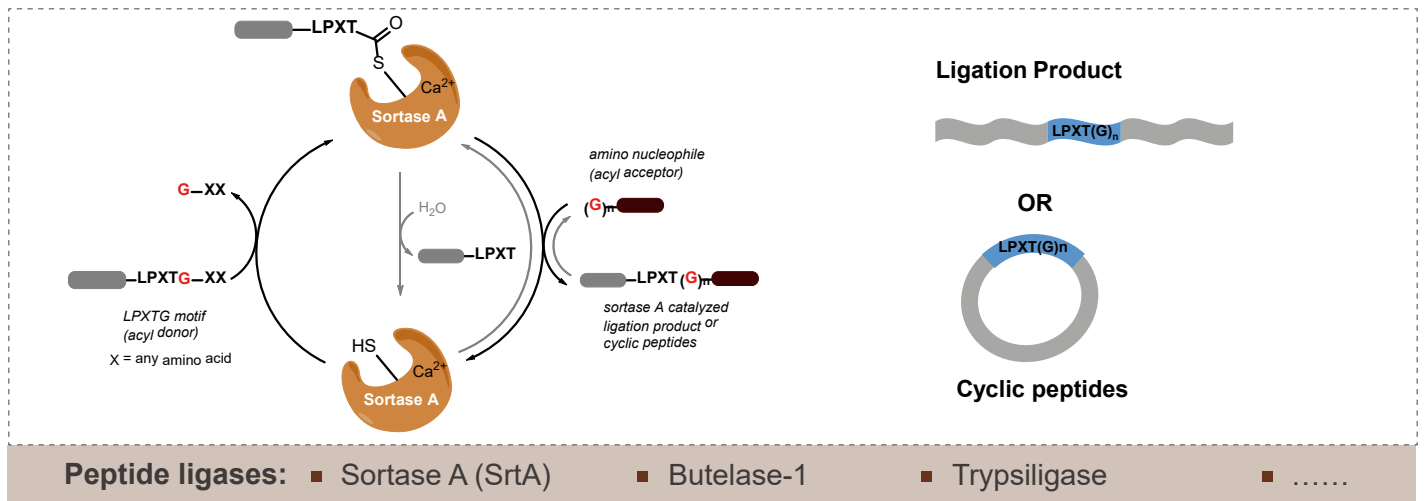
Enzyme Catalyzed unnatural amino acid synthesis



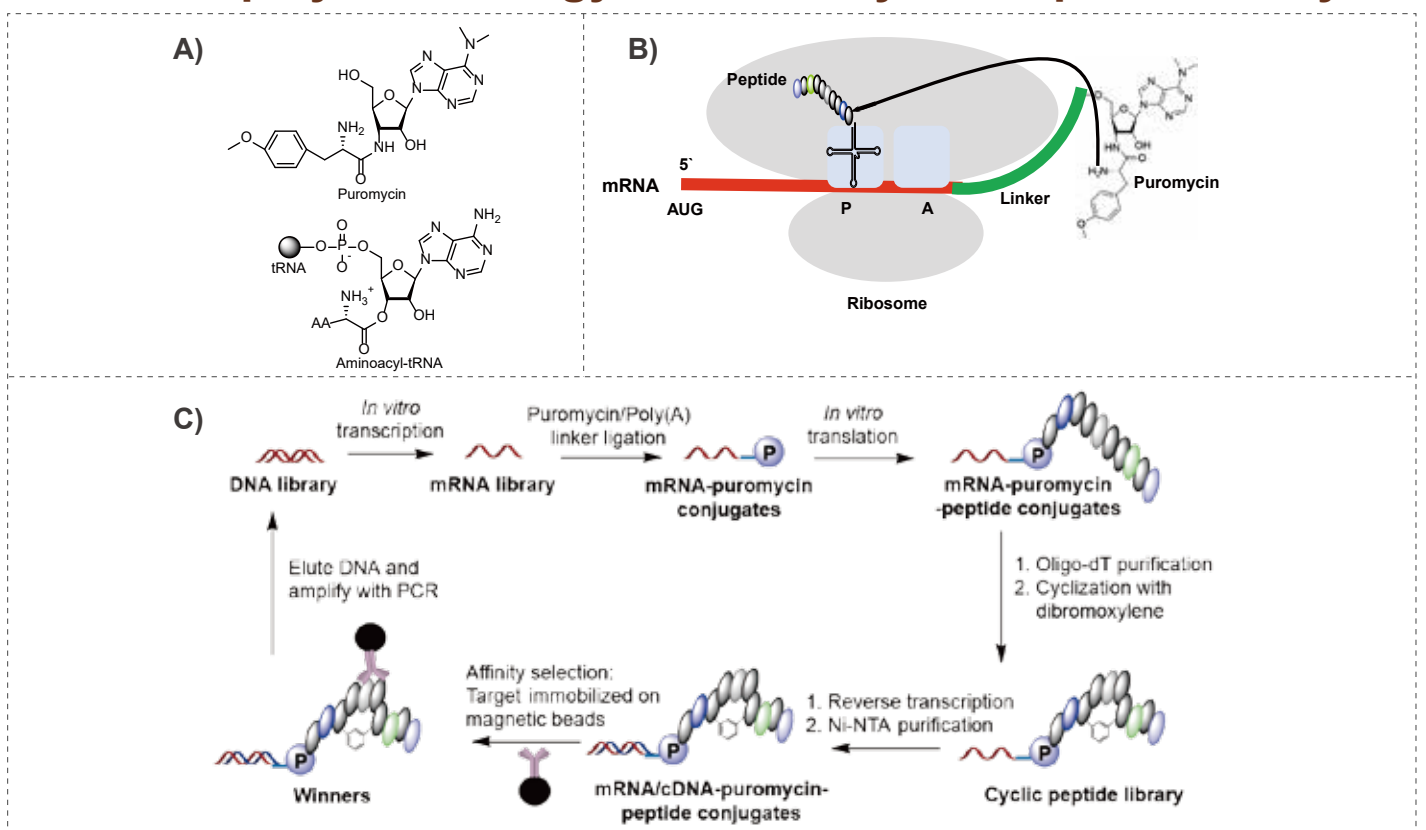
Enzyme evolution was applied to improve amino acid C-N lyase



Enzymatic Peptide Ligation & Cyclization



mRNA Display Technology for Macrocytic Peptide Library



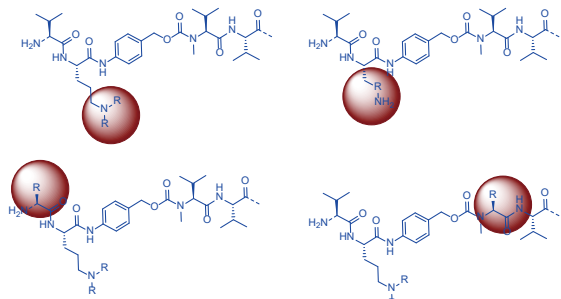
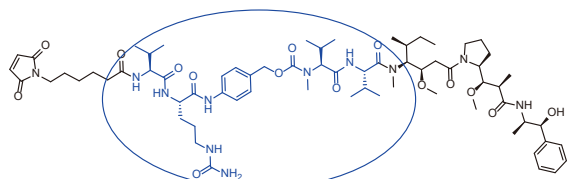
mRNA display technology for cyclic peptide library construction

- Library size exceeding 10^{13}
- Unnatural amino acids will be incorporated into the peptides through PURE cell-free translation system
- A typical round of an mRNA display selection takes 2-3 days
- Hits will be easily identified through sequencing of the cDNA linked with the peptide

Case Study

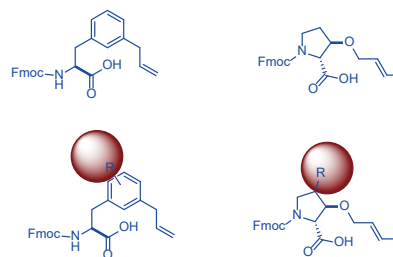
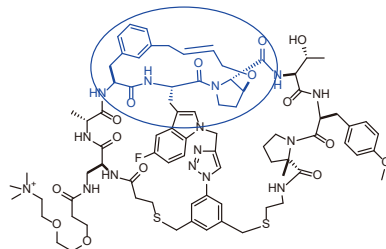
Medicilon Case: Peptide Synthesis

Amino acid modification and application in ADC drug



> 10 novel amino acid were made in Medicilon

Amino acid modification in PCSK9 peptide inhibitor synthesis



> 20 novel amino acid were made in Medicilon

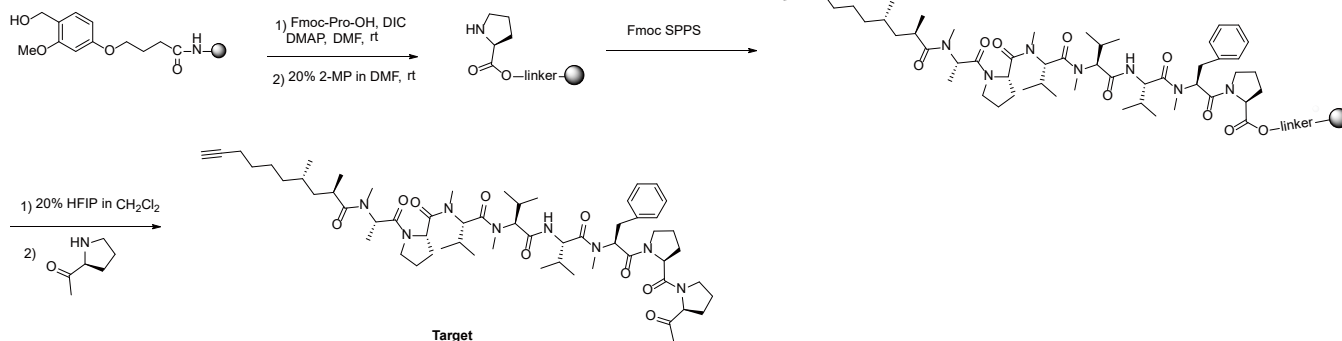
Medicilon Case: Solid-Phase Synthesis of Peptide



Peptide synthesizer

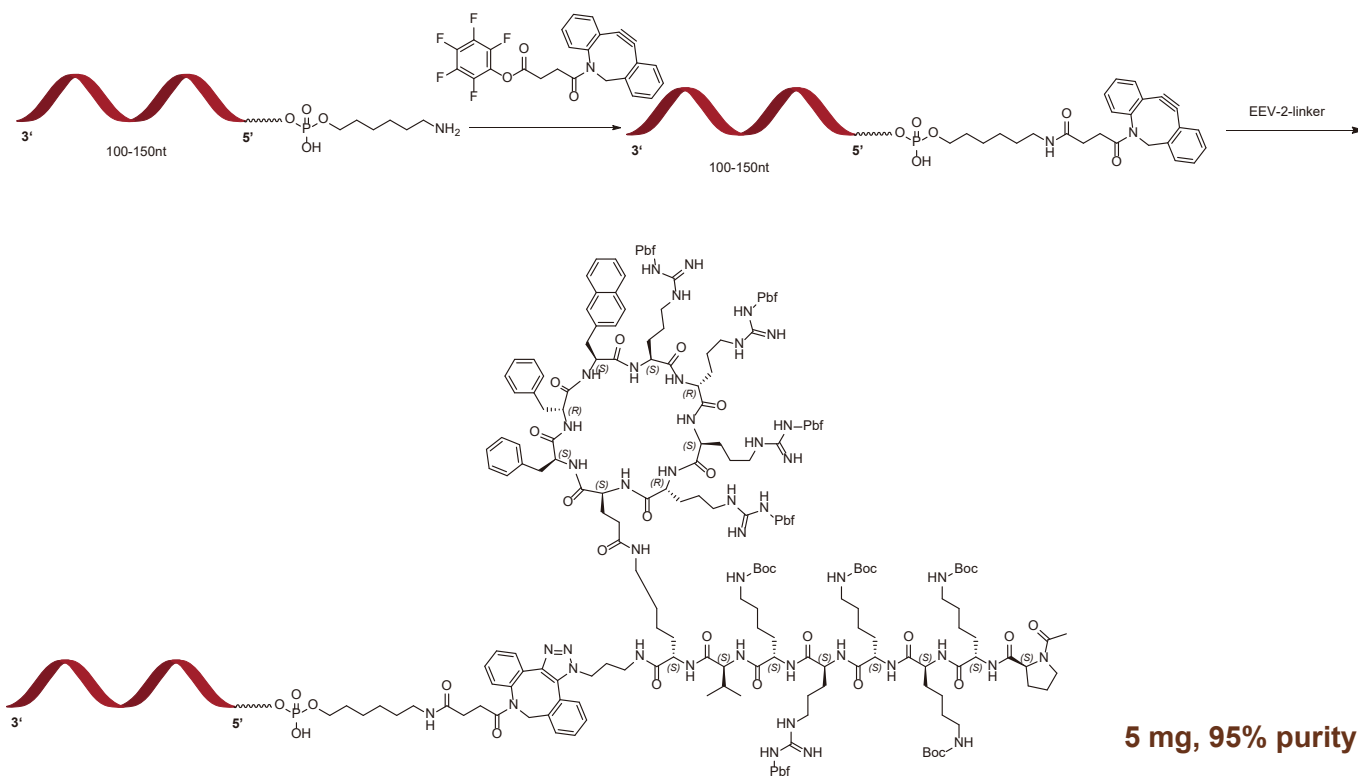


Peptide HPLC purification system



- Medicilon successfully made the reference compound in 2 weeks
- The purity of the desired compound is >98%
- The amount of the final peptide >500 mg

Medicilon Case: Synthesis of AOC



Peptide Bio-analysis

LC-MS/MS and High Resolution MS (GLP and non-GLP): all Waters



ACQUITY PREMIER UPLC



Triple Quad 6500+



XevoTQ-XS



MEDICILON

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