Integrated design of antibodies for systems biology using AbDesigner

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What problem does the AbDesigner solve?

- Lack of open-source, interactive, and artificial intelligence-based software for design of peptide-directed antibodies against whole proteome of organisms which facilitates studies at systems biology level
Custom antibody production

Protein of interest

AQP2 water channel

AbDesigner
http://helixweb.nih.gov/AbDesigner/

Antigen design

Peptide antigen synthesis and conjugation with carrier

CWTSGQVEEYLDADD

Immunization

Antibody purification and characterization

AQP2

AQP1

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AbDesigner

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Antigen design

3D structure
Native, non-denatured epitopes
Continuous or Discontinuous

Predicted structure from primary sequence
Antigen design

3D structure

Native, non-denatured epitopes
Continuous or Discontinuous

Predicted structure from primary sequence
Antigen design

• **AbDesigner**
  - [http://helixweb.nih.gov/AbDesigner/](http://helixweb.nih.gov/AbDesigner/)
**Input:** AQP2_HUMAN  Swiss-Prot: P41181  Peptide Length: 15  Epitope Length: 7

**Ig-score rank:**
1: PPTDWEEREVRRQS [242-256]  
2: EPDTDEEREVRQ [241-255]  
3: GLEPDIDDEEREVR [239-253]  
4: LEPEPDDEEREVR [240-254]  
5: KLEPDDEEREVR [238-252]  
6: DTPDEEREVR [237-251]  
7: RQSVTELHSPQLF [253-267]  
8: RQSVTELHSPQLF [254-268]  
9: DTPDEEREVR [244-258]  
10: RQSVTELHSPQLF [254-268]  
11: REVRSSVELHSPQ [249-263]  

"Ig-score rank" shows peptides from most immunogenic to least.

**Uniqueness-optimized rank:**
2: RQSVTELHSPQLF [254-268]  
3: RGNDTDEEREVR [238-252]  
4: RQSVTELHSPQLF [253-267]  
5: REVRSSVELHSPQ [249-263]  
6: EREDPTDEEREVR [238-252]  
7: DTPDEEREVR [244-258]  
8: DTPDEEREVR [239-253]  
9: RQSVTELHSPQLF [255-269]  
10: RGNDTDEEREVR [237-251]  
11: REVRSSVELHSPQ [249-263]  

"Uniqueness-optimized rank" shows Ig-score ranks for peptides predicted to be specific for target protein.

**Conservation-optimized rank:**
1: PPTDWEERERVVRQ [242-256]  
2: EPDTDEEREVRQ [241-255]  
3: GLEPDIDDEEREVR [239-253]  
4: LEPEPDDEEREVR [240-254]  
5: KLEPDDEEREVR [238-252]  
6: DTPDEEREVR [237-251]  
7: RQSVTELHSPQLF [253-267]  
8: REVRSSVELHSPQ [249-263]  
9: DTPDEEREVR [244-258]  
10: RQSVTELHSPQLF [254-268]  
11: REVRSSVELHSPQ [249-263]  

"Conservation-optimized rank" shows Ig-score ranks for peptides predicted to be recognized in target protein in multiple species.
What is AbDesigner?

*AbDesigner* is a new software tool that predicts optimal sites along the primary sequence of individual proteins for production of peptide-directed antibodies.

It calculates and extracts information needed to make a prediction and displays standard predictors in an easy-to-view graphical output.
Immunogenicity score (Ig-score)

- Ig-score predicts immunogenicity of a peptide (ability of peptide to provoke an immune response).
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Uniqueness score
- Uniqueness score predicts specificity (to a targeted protein) of an antibody produced by a particular peptide.
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Uniqueness score
- Uniqueness score predicts specificity (to a targeted protein) of an antibody produced by a particular peptide.

Conservation score
- Conservation score predicts likelihood of multi-species recognition of an antibody produced by a particular peptide.
Immunogenicity score (Ig-score)
   ▪ Ig-score predicts immunogenicity of a peptide (ability of peptide to provoke an immune response).

Uniqueness score
   ▪ Uniqueness score predicts specificity (to a targeted protein) of an antibody produced by a particular peptide.

Conservation score
   ▪ Conservation score predicts likelihood of multi-species recognition of an antibody produced by a particular peptide.

Protein features
   ▪ Describes regions or sites of interest in the protein sequence such as:
      ▪ post-translational modifications
      ▪ binding sites
      ▪ enzyme active sites
      ▪ local secondary structure
      ▪ sequence conflicts
      ▪ other characteristics reported in literatures
Methods implemented by *AbDesigner*

**Immunogenicity score (Ig-score)**
- Kyte-Doolittle hydropathy
  

  - Modified Chou-Fasman secondary structure
    

**Uniqueness score**
- Pattern matching with other proteins in the same species

**Conservation: conservation score**
- Pattern matching with orthologous proteins in the other species

**Protein features**
- Data extraction from Swiss-Prot database
Immunogenicity Score

Hydropathy * P-Turn * tail bonus
Possible number of epitopes per peptide

Choice 1: PD T D W E E R E V
Choice 2: DT D W E E R EV R
Choice 3: TD W E E R EV R R
Choice 4: DW E E R EV R R R
Choice 5: WE E R E V R R R Q
Choice 6: EE R E V R R R Q S
Tandem pattern matching

# Identical Matches - 1
# Identical Matches - 2
# Identical Matches - 3
# Identical Matches - 4
# Identical Matches - 5
# Identical Matches - 6

“Uniqueness Score”
Pattern matching with other proteins in the same species

“Conservation score”
Pattern matching with the same protein in other species
## Comparison of *AbDesigner* to the other existing solutions

<table>
<thead>
<tr>
<th></th>
<th><strong>AbDesigner</strong></th>
<th><strong>DNASTAR</strong></th>
<th><strong>Protean</strong></th>
<th><strong>Gene Inspector</strong></th>
<th><strong>GenScript</strong></th>
<th><strong>Antigen Profiler</strong></th>
<th><strong>Abie Pro 3.0</strong></th>
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<tbody>
<tr>
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AbDesigner-3D
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Speculate on additional research uses, commercial potential and/or public health benefits.

*AbDesigner* can be used for large-scale design of peptide-directed antibodies against whole proteome of organisms which facilitates studies at systems biology level.
Thank you