IGFR Family Members are Immunologic Targets in Breast Cancer

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IGFR1 Regulation of Breast Cancer

- Increased proliferation
- Decreased apoptosis
- Increased invasion
- Enhanced metastatic potential
- Plays a role in both hormone and trastuzumab resistance

Both IGFBP-2 and IGF1R proteins are overexpressed in breast cancer

Pollack M et al Nat Rev Ca, 2004
Breast Cancer Patients Can Have Immunity to IGFBP-2

Goodell and Park et al, 2007
Prediction of Potential Class II Epitopes

IGFBP-2 Protein Sequence

1. SYFPEITHI
2. Propred
3. MHC-Thread
4. Average Binding matrix method
5. Rankpep

Salazar et al, Clin Ca Res, 2003
Park et al, 2007
T Cell Response to IGFBP-2 Peptides

- 10/14 (71%) peptides immunogenic
- 36% in breast cancer patients
- 50% in volunteer age matched donors
- 14% in both

Park et al, 2007
**Antigens spots / 250,000 PBMCs**

* * p<0.05
** ** p<0.005

12/20 (60%)  
No response

8/20 (40%)  
Response

Park et al, 2007
Immunogenic IGFBP-2 Peptides are Highly Homologous with Bacterial Antigens

<table>
<thead>
<tr>
<th>IGFBP-2 Peptides</th>
<th>Homologous protein</th>
<th>Protein source of species</th>
<th>% Homology with mouse IGFBP-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>p17-31</td>
<td>Candida albicans</td>
<td>67</td>
<td>0</td>
</tr>
<tr>
<td>p251-265</td>
<td>Pseudomonas aeruginosa</td>
<td>47</td>
<td>100</td>
</tr>
<tr>
<td>p190-204</td>
<td>Trypanosoma cruzi</td>
<td>73</td>
<td>93</td>
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<tr>
<td>p266-280</td>
<td>Lactobacillus reuteri</td>
<td>47</td>
<td>100</td>
</tr>
<tr>
<td>p291-305</td>
<td>Schistosoma japonicum</td>
<td>60</td>
<td>93</td>
</tr>
<tr>
<td>p8-22</td>
<td>Aspergillus oryzae</td>
<td>67</td>
<td>67</td>
</tr>
<tr>
<td>p235-249</td>
<td>Candida albicans</td>
<td>53</td>
<td>93</td>
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<tr>
<td>p164-178</td>
<td>Trypanosoma cruzi</td>
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<td>86</td>
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<tr>
<td>p307-321</td>
<td>Staphylococcus aureus</td>
<td>47</td>
<td>80</td>
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<tr>
<td>p109-123</td>
<td>Pseudomonas fluorescens</td>
<td>53</td>
<td>80</td>
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<tr>
<td>p213-227</td>
<td>Aspergillus oryzae</td>
<td>67</td>
<td>93</td>
</tr>
<tr>
<td>p99-113</td>
<td>Human, murine, canine IGFBP3, 4, 5</td>
<td>67-80</td>
<td>80</td>
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<tr>
<td>p67-81</td>
<td>Propionibacterium acnes</td>
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<td>0</td>
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<tr>
<td>p121-135</td>
<td>Pseudomonas aeruginosa</td>
<td>60</td>
<td>80</td>
</tr>
</tbody>
</table>

60% of responders “molecular mimicry”
IGFBP-2 Peptide Specific T Cell Lines Respond to Protein

p8-22 (67% homologous to mouse)

p251-265 (100% homologous to mouse)

p291-305 (93% homologous to mouse)

*  p<0.05
** p<0.005

Park et al, 2007
neu Transgenic Mice: Model of HER2$^{\text{high}}$/ER$^{\text{low}}$ Breast Cancer

Expression of both neu and murine IGFBP-2 and IGF1R

Boggio et al, JEM, 1998
IGFBP-2 Specific T Cells Inhibit Tumor Growth

** p<0.005, n=5-6 mice/group
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