Exclusive Opportunity

Human Protein Therapeutics in Oncology
Dr. Erwin Van Meir

Cory G. Acuff, Ph.D.
Senior Licensing Associate
### Unmet Need: P53 Pathway Therapeutic

<table>
<thead>
<tr>
<th>Unmet Need</th>
<th>Bystander Effect</th>
<th>Tumorigenicity Assay</th>
<th>Next Steps</th>
</tr>
</thead>
</table>

- **P53** - “Holy Grail” of tumor suppressor proteins
  - Cell cycle regulation is well understood
  - Regulates expression of pro-apoptotic and angiostatic proteins

- P53 expression is lost in most tumors

- P53 - “non-drugable”

“What is in the P53 mediated pathway that can be used to address tumorigenesis?”

12/6/2006
Paracrine Mediated Apoptosis

- P53 mediated bystander cell death following gene therapy and radiation
- 40% reduction in tumor size in xenograft models
- Localized effect
- Only small number of cells with active

Radiation/Gene Therapy

Effector cell

Bystander cell

Apoptosis
P53 regulated Secretome

What is X?

Increased levels of 34 proteins
Decreased levels of 16 proteins

12/6/2006
## Mediator of Bystander Effect

<table>
<thead>
<tr>
<th>Unmet Need</th>
<th>Bystander Effect</th>
<th>Tumorigenicity Assay</th>
<th>Next Steps</th>
</tr>
</thead>
</table>

### Gal-3
- 31kDa beta-galactoside binding galectin family
- Novel P53 mediated secretion mechanism
- Induces apoptosis in immune cells

![Diagram showing P53 activation and apoptosis](image)

**P53 Activation**

**Apoptosis**

**Effector cell**

**Bystander cell**

12/6/2006
## Invention

<table>
<thead>
<tr>
<th>Unmet Need</th>
<th>Bystander Effect</th>
<th>Tumorigenicity Assay</th>
<th>Next Steps</th>
</tr>
</thead>
</table>

### A. Western for tet-on sGal-3:

<table>
<thead>
<tr>
<th>sGal-3</th>
<th>Low #33</th>
<th>Med. #21</th>
<th>High #12</th>
</tr>
</thead>
<tbody>
<tr>
<td>L16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dox</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>sGal-3</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TSP-1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

### B. Soft-agar colony formation assay:

```
- Dox
  L16
  Low #33
+ Dox
```

### C. In vivo tumorigenicity assay:

- sGal-3-
- sGal-3+ (clone #12)

```
1 2 3 4 5 6 7 8 9 10 11 12
# of weeks post sGal-3 induction
```

```
0 500 1000 1500 2000 2500 3000
Average Tumor Volume (mm^3)
```

```
0 500 1000 1500 2000 2500 3000
Average Tumor Volume (mm^3)
```

```
Weeks post sGal-3 induction
```
Provisional application filed
September 2006

Claims address:
• Methods of modulating apoptosis
• Methods of treating disease (i.e., cancer)
## Further Development

<table>
<thead>
<tr>
<th>Unmet Need</th>
<th>Bystander Effect</th>
<th>Tumorigenicity Assay</th>
<th>Next Steps</th>
</tr>
</thead>
</table>

### Current Activities

1. *In vitro* evidence confirming Gal3 mediates Bystander effect
2. Early *in vivo* xenograft POP data

### Next Steps

1. Exogenous Gal3 administration in multiple xenograft models
2. Dosing effects