INTRODUCTION

- Differential expression of proteins between tumour and healthy vasculature introduces potential targets for anti-cancer treatments
- Nevertheless many therapies targeting vasculature are unsuccessful in the clinic and there is a need for better characterization of these molecules
- CLEC14A is a novel tumour endothelial marker
  - It is highly expressed on vasculature of wide range of solid tumours (plasma membrane protein)
  - It has a role in cell migration and filopodia formation
  - It is expressed under low shear stress conditions

KEY FINDINGS – CLEC14A KNOCK OUT MICE

- Loss of CLEC14A in mice impairs sprouting angiogenesis in aortic ring assay and vascularization of sponge barrels implanted subcutaneously (Figure 1)
- CLEC14A knock out mice show reduction in tumour growth and vascularization (Figure 2)

AIMS

Characterization of CLEC14A intracellular domain function

Identification of CLEC14A intracellular domain binding partners and signaling pathways

Table 1 Mass spectrometry results

<table>
<thead>
<tr>
<th>Protein</th>
<th>Size (kDa)</th>
<th>Peptide hits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myosin 9</td>
<td>227</td>
<td>11</td>
</tr>
<tr>
<td>Moesin</td>
<td>68</td>
<td>3</td>
</tr>
<tr>
<td>Myosin 10</td>
<td>200</td>
<td>2</td>
</tr>
<tr>
<td>T-complex protein 1 subunit eta</td>
<td>59</td>
<td>2</td>
</tr>
<tr>
<td>Clathrin heavy chain 1</td>
<td>188</td>
<td>2</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- CLEC14A induces filopodia formation in HEK293T cells
- Deletion of intracellular domain of CLEC14A does not affect filopodia formation
- Possible intracellular binding partners of CLEC14A are involved in cell migration and actin cytoskeleton reorganization

References: