*UWA technology licensing/ partnering opportunity:*

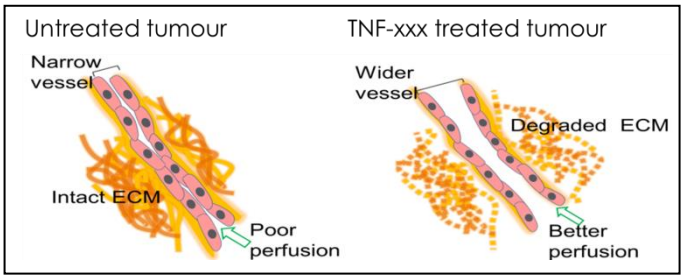
# Tumour ECM-targeted Tumour Necrosis Factor (TNF) alpha

## Background:

Solid tumours may be 10 times stiffer than normal tissue. Tumour stiffness is a result of aberrant overgrowth of extra cellular matrix (ECM) components. High tumour-ECM content of solid tumours acts to constrict blood vessels and limit tumour perfusion, presenting a barrier to delivery of activated immune cells and circulatory agents to the tumour microenvironment (TME).

Now researchers at UWA have developed a novel immuno-modulatory agent, exploiting highly selective affinity of a small homing peptide 'CSG' for tumour-ECM; TNF-CSG stimulates local activation of native immune cells, leading to tumour-ECM degradation, significantly reduced tumour stiffness and interstitial pressure, and increased tumour perfusion.

Used as an adjunct therapy TNF-CSG has the potential to increase efficacy and reduce toxicity of chemo- and immunotherapy drugs (and to enhance tumour detection by imaging agents). In addition TNF-CSG has direct anti-cancer activity as a monotherapy.




## Advantages:

- Reduced tumour stiffness, interstitial pressure and increased tumour perfusion shown by OCT/ micro-elastography and DCE-MRI, in 4T1 breast, CT26 colon and RIP-Tag pancreatic tumour models.
- TNF-CSG has tumour-specific activity; comparator PEGPH20 (Halozyme), a hyaluronidase-based drug enzymatically degrades hyaluronan; a ubiquitous ECM component.
- Enhanced tumour-uptake of doxorubicin and iron-oxide micelles (for MRI/ PET imaging).
- Monotherapeutic activity: reduced tumour growth, and tumour clearance associated with immune cell activation and infiltration, and increased cytotoxic T-cell abundance.
- Reduced secondary metastasis in a 4T1 mouse model – no loss of containment effect.
- No signs of systemic toxicity; native TNF (2µg, IV) resulted in death of 6/6 mice after 2 doses; TNF-CSG had no cytotoxic effects after 20 doses (2µg, IV) over 10 wks.

## A highly differentiated drug candidate:

- There is no other known agent which acts to stimulate native immune cells in the TME to degrade aberrant ECM and increase delivery of circulatory agents.
- TNF-CSG has activity as a monotherapy owing to immune cell activation and infiltration.
- An 'immuno-mechanical' approach suited to combination with checkpoint blockade and chemotherapy agents.

## Intellectual property:

A PCT phase application was filed January 2017 claiming a TNF-CSG biomolecule and methods of use. All claims are reported by the ISR and Written Opinion to be novel and inventive.

## Commercialisation:

We are seeking licensing interest to undertake further preclinical and clinical development of this program. For further information please contact:

Dr Louis Pymar, Commercialisation Manager, Research Development and Innovation
E: louis.pymar@uwa.edu.au | T: +61 8 6488 4363