Antibody Clamp for enhanced immunotherapy agonism

The Ab Clamp is a novel, simple & flexible plug-&-play technology with potential to increase Ab agonism for cancer immunotherapy

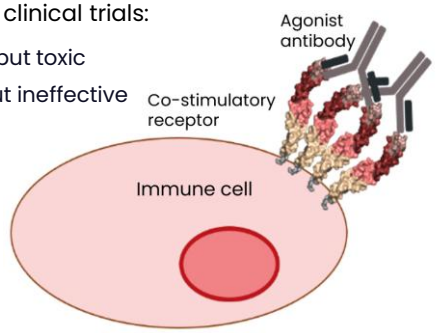
- Restricts Fab arm mobility via simple mutations
- More compact Abs increase receptor clustering and agonism
- Can be deployed in any isotype and any antibody

Problem: Cancer immunotherapy needs new approaches

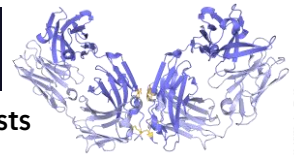
- Immunotherapies have revolutionised cancer treatment, through targeting inhibitory immune receptors (e.g. PD-1)
- But progress has stalled & their efficacy is limited
  - 70-80% of cancer patients are ICI unresponsive

Approach: Immunostimulatory antibodies (ISAs)

- Target and bind co-stimulatory receptors expressed on immune cells to elicit agonistic effects, resulting in:
  - Boosted anti-tumour immune responses
  - Synergy with ICIs
- BUT, many ISAs are stalling in clinical trials:
  - Urelumab = effective but toxic
  - Utomilumab = safe but ineffective
- Therefore, there is an unmet need for more agonistic & less toxic ISAs



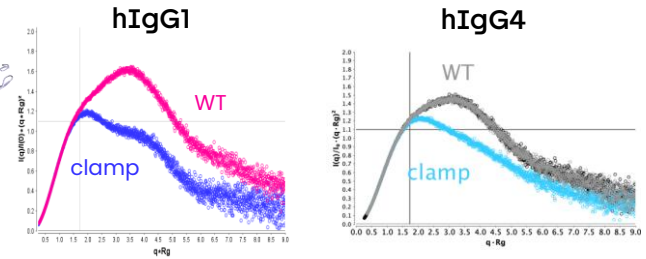
Solution: Ab Clamp unlocks powerful & safe agonists



- Ab Clamp involves simple Ab modifications
- Clamped ISAs are potentially more effective and less toxic
- Ab Clamp can be applied to evoke agonism across isotypes in a wide range of targets
- Simpler to implement than other Ab engineering methods
  - Avoids increased instability, immunogenicity and clearance observed with Fc region Ab modifications
- Potential to synergise with other Ab engineering methods
  - e.g. bispecificity/multi-valency

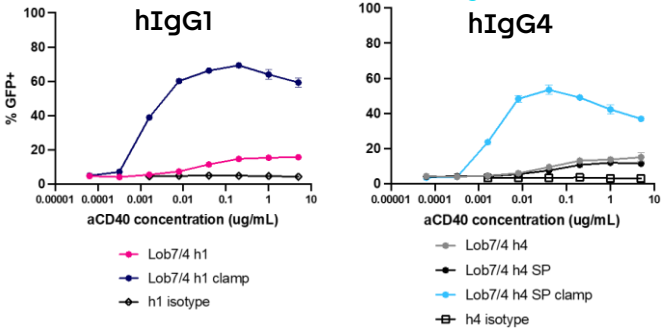
Technology Stage of Development

- Ab Clamp has been successfully applied to reduce flexibility of multiple ISAs to receptors in the TNFR and IgSF families:
  - CD40, 4-1BB, OX40, CD27 & CD28
- POC data validates that Clamped ISAs elicit increased agonism
- Compelling *in vivo* data demonstrating improved agonism of Clamped v WT Chi Lob 7/4 (CD40)
- Awarded the 2025 CRH Translational Fund to perform head-to-head comparison experiments:
  - PK and efficacy for Clamped v WT Urelumab (4-1BB) and Chi Lob 7/4 (CD40) in CRC tumour model
  - Toxicity of Clamped vs WT 4-1BB ISAs in a PBMC humanized mouse model (versus Urelumab)
  - Benchmarking increased Ab agonism against other Ab engineering approaches



SAXS shows Clamp restricts Ab flexibility

Which evokes increased Ab agonism



Opportunity Summary

Seeking: partners for co-development/licensing, including those with stalled or in-development ISAs

IP: protected by Dec 2024 PCT filing - covers all isotypes & a broad range of receptors (e.g. CD40, 4-1BB, CD28, CD27, DR4, DR5)

- Background IP in Ab engineering (*PCT/IB2015/052166*) & 4-1BB/OX40 Abs (*PCT/EP2016/076747*)

Team: research group are world specialists in antibody engineering

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FURTHER FASTER TOGETHER
We are beating cancer

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