Multi-targeting of tumour cells using the common light chain antibody format

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The Future of Antibody Therapy ...

MeMo®
Biclonics™
Biclonics™ ENGAGE
Oligoclonics®

Presentation Overview

- Common light chain human mAbs – Rationale
- Merus Biclonics™ technology
- MeMo®, a powerful transgenic mouse antibody platform

Common light chain human mAbs

Panel of conventional mAbs:
- diversified heavy chain
- diversified light chain

Panel of common light chain mAbs:
- diversified heavy chain
- identical light chain

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Why is the common light chain (cLC) important?

The cLC format facilitates multispecific formats because it allows single cell expression without V\_H/V\_L mispairing.

Single Cell Expression common light chains

- 25%
- 25%
- 50%

Biclonics™
CH3 Technology

Production of pure bispecifics: Biclonics™ from a single cell

Merus proprietary CH3 Technology

common light chain bispecific human antibody = Biclonics™

CLEC12A x CD3 — Biclonics™ engager is highly potent

HL60 cytotoxicity assay with human T cells

Effector to target ratio 5:1, 10% HD
Superior *in vitro* functional activity of Biclonics

**EGFR x HER3 Biclonics Leads**

<table>
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<tr>
<th>Name</th>
<th>IC50 [pM]</th>
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<tbody>
<tr>
<td>M61</td>
<td>12.5</td>
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<tr>
<td>M3A2</td>
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<tr>
<td>MEH7945A</td>
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>20-fold more potent Biclonics™

*bxPC3 assay in the presence of heregulin and EGF*

Manufacturing by conventional IgG production

- Single manufacturing cell-line
- No need for two manufacturing cell-lines and dissociation/re-association processes
- Conventional full-length human IgG: standard production/purification

MeMo®

MeMo®: for panels of high quality common light chain human antibodies

MeMo® design

- Knock out of endogenous murine Ig loci
- Insertion of rearranging human V<sub>H</sub> locus and a single human light chain

**Merus – VARI december 2012**
MeMo® delivers high quality human IgG panels

- Highly distinct panels of antibodies isolated
  - Sequence diversity different immunization protocols
  - Epitope diversity for all targets including functional sites

- MeMo-derived IgG have a range of affinities from low nM to pM

- Functional IgG identified with potent tumour growth inhibitory activity

- MeMo-derived IgG show attractive biochemical and biophysical properties

Acknowledgements