Novel anti CD44 antibody with unique mode of action

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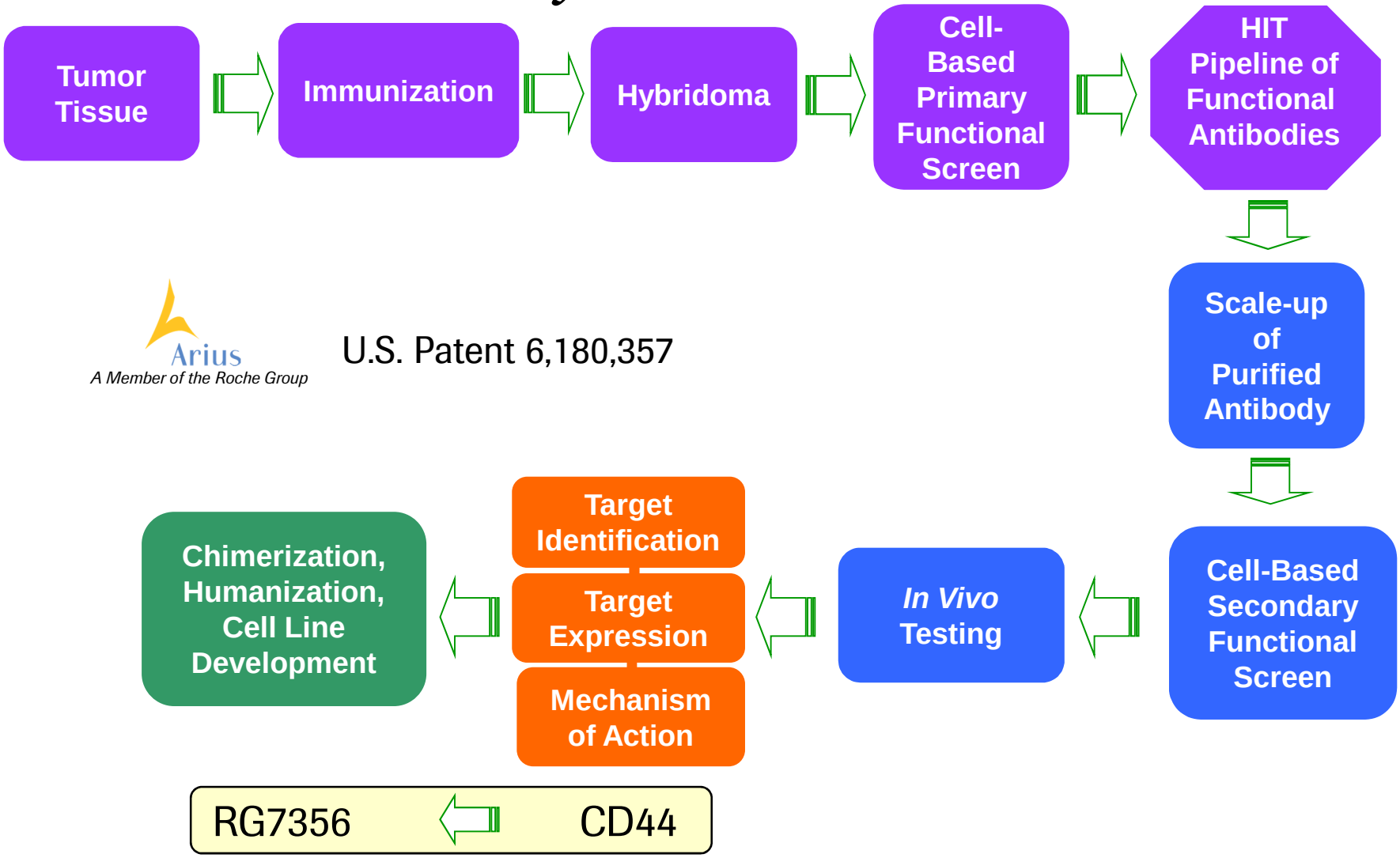
Discovery of the anti-CD44 mAb RG7356

FunctionFIRST™ Platform



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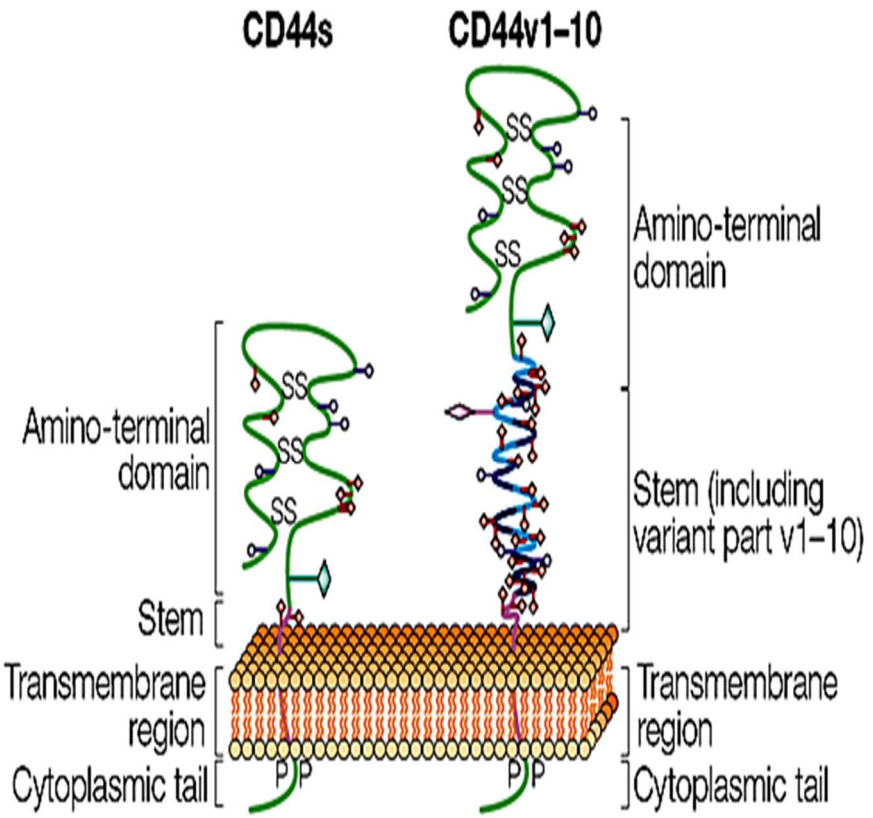
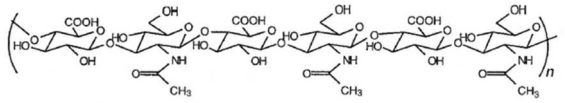
U.S. Patent 6,180,357

CD44 receptor

- CD44 is a single-chain, single-pass transmembrane glycoprotein
- CD44 is overexpressed in many solid tumors and hematological malignancies, but also present on immune effector cells
- Principal ligand: hyaluronic acid (HA)
  - overexpressed at site of inflammation
  - HA rich tumors attract and educate Mϕ[1]
- CD44 and/or HA overexpression is linked to increased metastasis and reduced survival for a panel of cancers[2]





HA showing three disaccharide repeat units

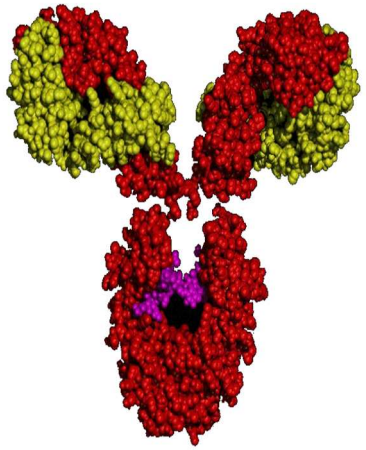
[1]*Clin. Cancer Res., 2009, 15, 7462-7468 and J. Biol. Chem. 2011, 286, 19179-19190*

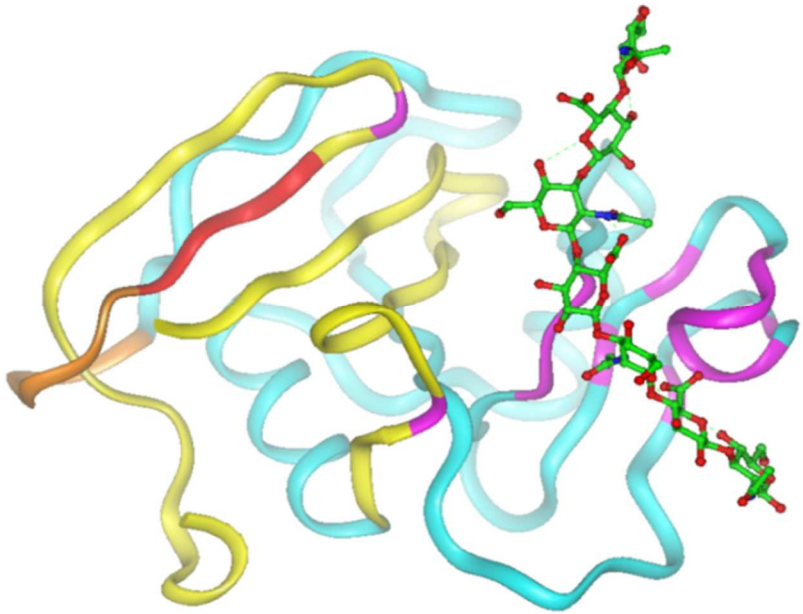
[2]*Nature Rev. Cancer, 2011, 11, 254-267*

RG7356

Novel α-CD44 mAb that targets a unique epitope on CD44

- Humanized IgG1 κ, cross-reactive to *Cynomolgus* monkey, but not to murine CD44





HA binding site*
RG7356 binding epitope
Overlapping residues

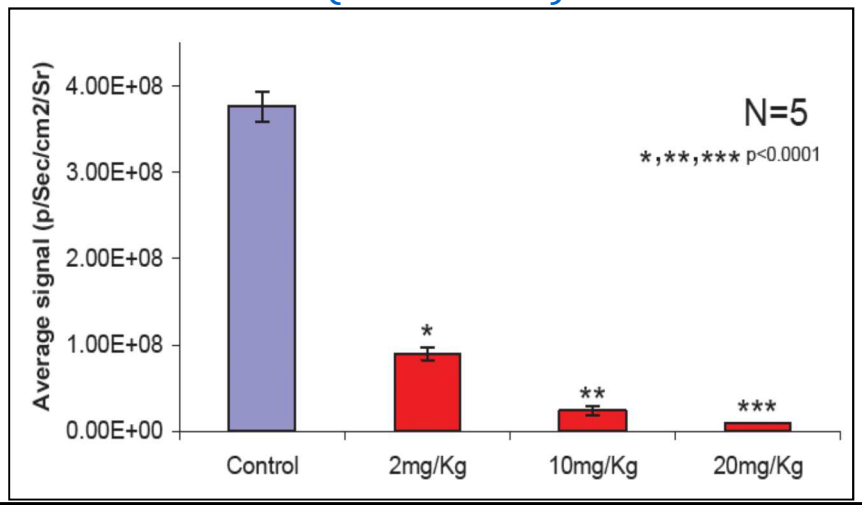
- RG7356 binds to the constant region of CD44 in a loop that is spatially close to the HA binding domain
- RG7356 binds to sCD44 and splice variants

* *JCB, 1993, 122 (1): 257*

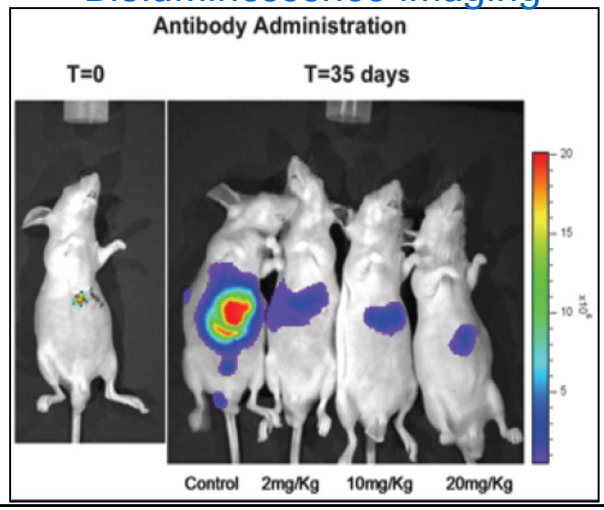
Metastatic hepatocellular carcinoma

Highly aggressive patient-derived, orthotopic HCC model

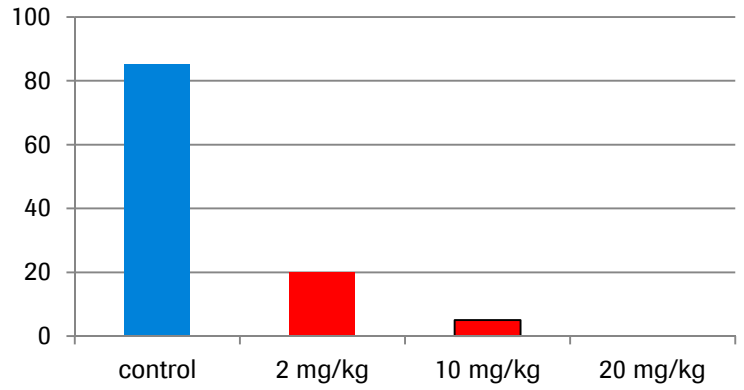
MHCC-97H (CD44⁺/HA⁺): TGI



Bioluminescence imaging

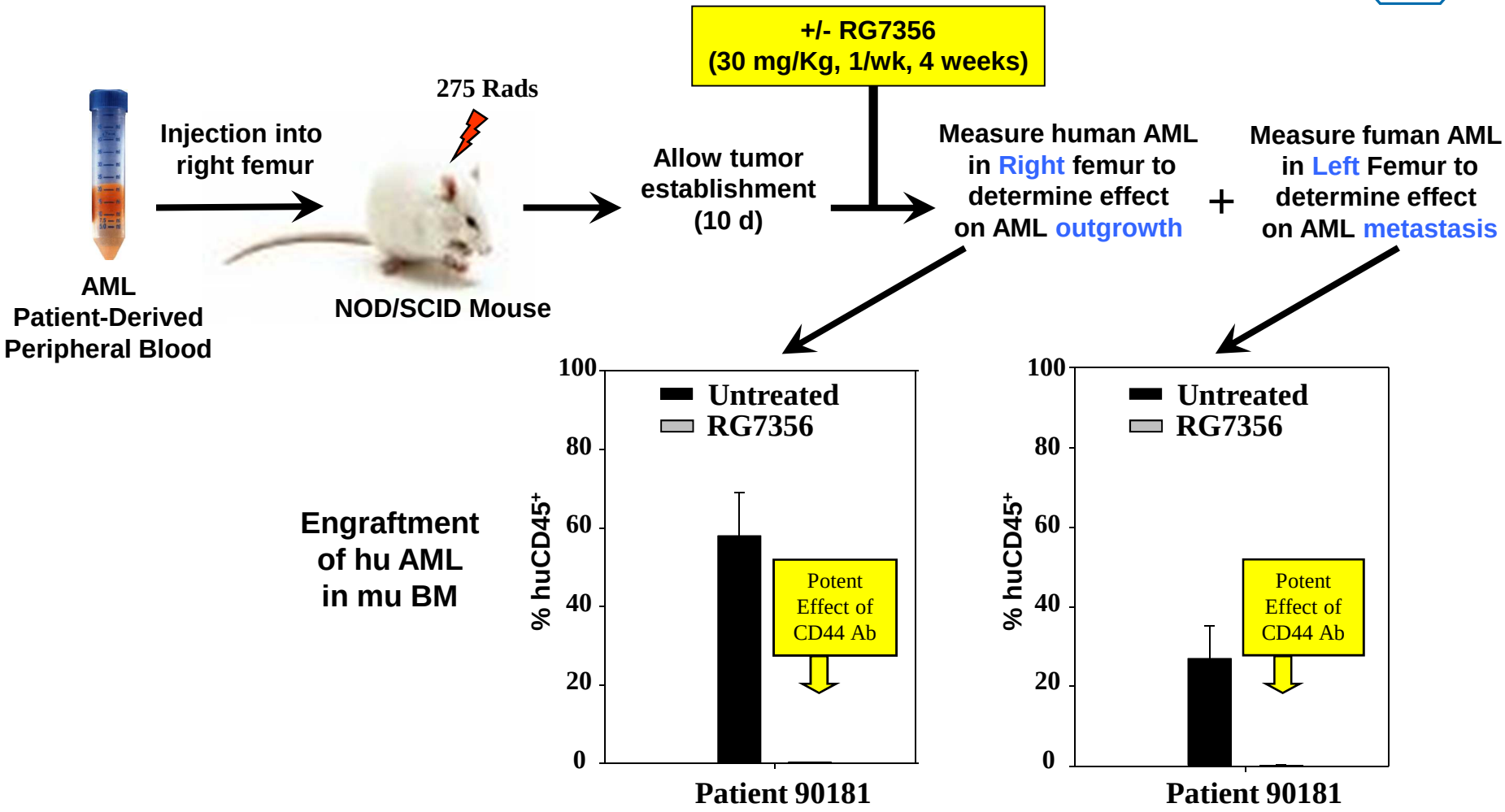


Frequency of metastasis occurrence in treated vs. untreated mice (lung, intrahepatic, intestine, urinary)



- Dose dependent inhibition of primary tumor growth & metastasis formation

Efficacy in patient-derived, orthotopic AML model



- RG7356 inhibits outgrowth in 7/9 and metastasis in 9/9 human AMLs[1]

[1] *Collaboration with J. Dick, Univ. Toronto, Toronto, Canada; one out of 9 patients samples shown*

Summary: αCD44 mAb RG7356

- RG7356 triggers direct anti-tumor effects by activation of macrophages to phagocytose $CD44^+$ tumor cells
- RG7356 inhibits migration/homing/metastasis of tumor cells in the in the HA-rich environment (e.g. bone marrow niche)

➢ Efficacy is mainly driven by interference with CD44-HA interactions and activation of macrophages for phagocytosis

- RG7356 shows an excellent safety profile in *Cynomolgus* monkey GLP toxicology studies and a favorable biodistribution in imaging studies in *Cynomolgus* monkeys and man

➢ Clinical development of RG7356 in solid tumors and hematological malignancies is underway

Acknowledgements

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- Current and former CD44 project team

Thanks for your attention!