Human Anti-Nucleolin Antibodies with Broad Spectrum Anticancer Activity

Daniel J. Fernandes(1,2), Yoko Otake(1), Natalie A. Sutkowski(2) and Robert L. Capizzi(1)

(1) CharlestonPharma, LLC, Charleston, SC. (2) Medical University of South Carolina, Charleston, SC.

BACKGROUND

Nucleolin

- Nucleolin is a multifunctional phosphoprotein that is highly overexpressed in the plasma membrane and cytoplasm of most tumor cells, but is usually undetectable on the surface of normal cells.
- Overexpression of nucleolin on the surface of many types of tumor cells accounts for the broad-spectrum anti-tumor activity of the anti-nucleolin HuMAbs.
- Anti-nucleolin HuMAbs gain intracellular access possibly by nucleolin-mediated endocytosis.

Human Antibody Technology

RESULTS

Broad-Spectrum Anti-Cancer Activity

Figure 6. Nucleolin Specific Killing of MCF-7 Breast Cancer Cells Occurs Without Toxicity to MCF-10A Normal Mammary Cells. (A) Surface and cytoplasmic over-expression of nucleolin can be determined in MCF-7 vs MCF-10A cells. Nucleolin were counter-stained with propidium iodide. Cell morphology is shown as DIC images. (B) MCF-7 breast cancer and MCF-10A normal mammary epithelial cells. (Graudins et al. Cancer Res. 2008, 68(9).) (B) MDA-MB-231 breast cancer cells. Results are representative of three experiments.

Figure 7. Effects of CP101 and CP201 HuMAbs on the Growth of Prostate and Pancreatic Cancer Cells. Growth inhibition was determined as described in Figure 5. Results are means of 4 experiments ± SD.

CONCLUSIONS

- The fully human anti-nucleolin HuMAbs CP101 and CP201 bind tightly to human recombinant nucleolin and to nucleolin on the surface of tumor cells.
- CP101 and CP201 can kill tumor cells independently of CDC and HDCC although complement increases the rate of cell killing.
- Direct tumor cell killing by CP101 and CP201 is consistent with intracellular uptake of the HuMAbs.
- The broad spectrum activity and high tumor cell selectivity of CP101 and CP201 against common solid tumors and acute leukemias suggest that anti-nucleolin HuMAbs have a large market potential.

ACKNOWLEDGEMENTS

Research supported by a HCC Translational Research Grant, NCI grant CA109254-51, DOD grant BC111966, and a grant from South Carolina Launch.