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## **Lecture 4: Cell Targeting and its Evaluation**

- 4.1 Overview: targeting nanosystems to cells
  - 4.1.1 antibody targeting
  - 4.1.2 peptide targeting
  - 4.1.3 aptamer targeting
  - 4.1.4 ligand-receptor targeting
- 4.2 Antibodies polyclonal and monoclonal
  - 4.2.1 Where do antibodies come from in nature?
  - 4.2.2. How do we make them in the laboratory?
  - 4.2.3 Monoclonal antibodies some details you need to know!
  - 4.2.4 Labeling strategies
  - 4.2.5 Therapy problems with mouse monoclonal antibodies
  - 4.2.6 "Humanizing" monoclonal antibodies to reduce adverse host immune reactions
  - 4.2.7 Why antibodies may not be a good overall choices for targeting nanosystems to cells
- 4.3. Peptide targeting
  - 4.3.1 How does a peptide target?
  - 4.3.2 Examples of peptide targeting
  - 4.3.3 Creating new peptides by random peptide phage display libraries
  - 4.3.4 High-throughput screening of those peptide libraries
  - 4.3.5 Advantages and disadvantages of peptide targeting
- 4.4 Aptamer targeting
  - 4.4.1 What are aptamers and how do they target?
  - 4.4.2 Some different types of aptamers
  - 4.4.3 How do you make aptamers?
  - 4.4.4 How do you screen for useful aptamers?
- 4.5. Ligand-receptor targeting
  - 4.5.1 What are ligands?
  - 4.5.2 What are their advantages/disadvantages?
  - 4.5.3 Example folate receptors
- 4.6 How do we quantitatively evaluate targeting?
  - 4.6.1 Technologies for evaluating targeting
    - 4.6.1.1 Flow cytometry
    - 4.6.1.2 Scanning image cytometry
  - 4.6.2 Evaluating targeting specificity
  - 4.6.3 Evaluating targeting sensitivity

## **Lecture 4 References**

- 1. Leary, J.F.: "Strategies for Rare Cell Detection and Isolation" In: Methods in Cell Biology: Flow Cytometry (Edited by Z. Darzynkiewicz, J.P. Robinson, H.A. Crissman), vol. 42: pp. 331-358, 1994.
- 2. Leary, J.F. "Ultra High Speed Cell Sorting" Cytometry Part A 67A:76-85 (2005)
- 3. Rosenblatt, J.A., Hokanson, J.A., McLaughlin, S.R., Leary, J.F.: A Theoretical Basis for Sampling Statistics Appropriate for the Detection and Isolation of Rare Cells Using Flow Cytometry and Cell Sorting Cytometry 27: 233-238; 1997.
- 4. Prow, T.W., Kotov, N.A., Lvov, Y.M., Rijnbrand, R., Leary, J.F. "Nanoparticles, Molecular Biosensors, and Multispectral Confocal Microscopy" Journal of Molecular Histology, Vol. 35, No.6, pp. 555-564, 2004.
- 5. Szaniszlo, P., Rose, W.A., Wang, N., Reece, L.M., Tsulaia, T.V., Hanania, E.G., Elferink, C.J., Leary, J.F. "Scanning Cytometry with a LEAP: Laser-Enabled Analysis and Processing of Live Cells In Situ" Cytometry 69A: 641-651, 2006.
- 6. von Maltzahn, G., Ren, Y., Park, J-H, Min, D-H, Kotamraju, V.R., Jayakumar, J., Fogal, V., Sailor, M.J., Erkki Ruoslahti, E., Bhatia, S.N. "In ViVo Tumor Cell Targeting with "Click" Nanoparticles". Bioconjugate Chem. 19, 1570–1578 (2008)
- 7. McCarron, P.A., Marouf, W.M., Quinn, D.J., Fay, F., Burden, R.E., Olwill, S.A., Scott, C.J. "Antibody Targeting of Camptothecin-Loaded PLGA Nanoparticles to Tumor Cells". Bioconjugate Chem. 19, 1561–1569 (2008).
- 8. Yang, X., Bassett, S.E., Li, X., Luxon, B.A., Herzog, N.K., Shope, R.E., Aronson, J., Prow, T.W., Leary, J.F., Kirby, R., Ellington, A.D., Gorenstein, D.G.: "Construction and selection of bead bound combinatorial oligonucleoside phosphorothioate and phosphorodithioate aptamer libraries designed for rapid PCR-based sequencing" Nucleic Acids Research 30 (23)e132: 1-8, 2003.
- 9. Yang, X., Li, X., Prow, T.W. Reece, L.M., Bassett, S.E., Luxon, B.A., Herzog, N.K., Aronson, J., Shope, R.E., Leary, J.F., Gorenstein, D.G. "Immunofluorescence Assay and Flow Cytometric Selection of Bead Bound Aptamers" Nucleic Acids Research 31 (10): 1-8, 2003
- 10. Ellington Lab Aptamer Database: <a href="http://aptamer.icmb.utexas.edu/index.php">http://aptamer.icmb.utexas.edu/index.php</a>
- 11. Lu, Y., Low, P.S. "Folate-mediated delivery of macromolecular anticancer therapeutic agent". Advanced Drug Delivery Reviews 54: 675–693 (2002).
- 12. Shapiro, H.M. Practical Flow Cytometry 4<sup>th</sup> edition 2003.