BIOSCIENCE IN THE 21ST CENTURY

HIGHLIGHTS AND FUTURE PROSPECTS

VASSIE C. WARE, Ph.D.
LEHIGH UNIVERSITY

MULTIDISCIPLINARY APPROACHES

BIOLOGICAL ENGINEERS

BIOCHEMISTS

NEUROBIOLOGISTS

MOLECULAR BIOLOGISTS

MICROBIOLOGISTS

CHEMISTS

CLINICIANS

CELL BIOLOGISTS

VIROLOGISTS

BIOETHICISTS &
MEDICAL HUMANISTS

PHYSICISTS

MECHANICAL ENGINEERS

COMPUTER SCIENTISTS

PROBLEMS IN BIOSCIENCE

Genomics and Genomic Technologies

Drug Delivery

Ethical and social implications

Obesity

Cardiovascular Disease

Neurological Disease

Behavioral disorders

Infectious Diseases

Stem Cells and Regenerative Medicine

Cancer

Recent advances:

Genomics and Genomic Technologies

- understanding microbial genomes for biomedical applications and biofuel/bioremediation applications
- drug development prospects
- pharmacogenomics

Stem Cell Biology

- tracking stem cells in the brain to understand neurological disease
- understanding disease mechanisms in the laboratory
- drug development prospects

Ethical Considerations

APPLICATIONS OF GENOMICS AND GENOMICS TECHNOLOGIES

First Bacterial Genome Transplantation Changes One Species To Another

(*Science,* August 2007)

Changed one bacterial species, *Mycoplasma capricolum* into another, *Mycoplasma mycoides* Large Colony (LC), by replacing one organism's genome with the other one's genome.

WHY?

…"We are committed to this research as we believe that synthetic genomics holds great promise in helping to solve issues like climate change and in developing new sources of energy."

ETHICAL AND SOCIAL CONCERNS?

In collaboration with the Center for Strategic & International Studies (CSIS), and the Massachusetts Institute of Technology (MIT), the Venter group is exploring the risks and benefits of this emerging technology, as well as possible safeguards to prevent abuse, including bioterrorism.

http://www.sciencedaily.com/releases/2007/06/070628232413.htm

APPLICATIONS OF GENOMICS AND GENOMICS TECHNOLOGIES

MICROBIAL GENOMICS PROJECTS:
www.ncbi.nih.gov

1995 : the first genome sequence of a free-living organism, the bacterium *Haemophilus influenzae,* was completed.

1997: *E. coli* genome sequence completed

610 microbial genomes completed as of 12/2007
902 microbial genomes in progress as of 12/2007

DISCUSSION:

What technologies have assisted in the completion of these projects?

Improvements in sequencing and bioinformatics technologies

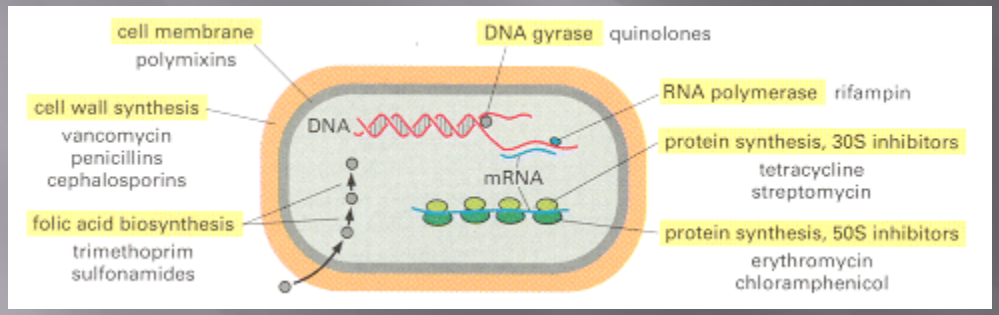
What is the value of these genomics projects?

Comparisons between pathogens and commensals to determine genomic islands that confer pathogenicity to determine possible targets for anti-microbial therapies, vaccine development, etc.

New Developments in Antibiotics

The Problem:

- **Very few new antibiotics in the pharmaceutical pipeline**
- **Increasing resistance of pathogens to existing antibiotics**
- **Few new targets to pursue for antibiotic development**



Molecular Biology of the Cell by Alberts et al. 2002

Structural Insight into the Transglycosylation Step of Bacterial Cell-Wall Biosynthesis Andrew L. Lovering, Liza H. de Castro, Daniel Lim, and Natalie C. J. Strynadka (9 March 2007) *Science* **315** (5817), 1402. [DOI: 10.1126/science.1136611]

Applications of Genomics and Genomics Technologies

Pharmacogenomics:

The study of how variations in the human genome affect the response to medications; implications for "individualized-drug therapies".

New tests approved by the FDA can allow clinicians to genetically test for patients who may be low- or high-responders to certain drugs. Technologies include the use of DNA microarrays to determine expression patterns.

DISCUSSION:

How effective are these tests and what might the ethical implications be?

Stem Cell News

"Scientists Find Way to Track Stem Cells in Brain"
(*Science,* November 2007)

"Stem Cells Restore Memory in Mice"
(*Journal of Neuroscience,* October 2007)

"Researchers Isolate Adult Stem Cells for First Time in Tendon"
(*Nature Medicine,* September 2007)

" Stem Cells From Testes Produce Wide Range of Tissue Types"
(*Nature,* September 2007)

"Scientists Turn Human Skin Cells into Stem Cells"
(*Science*; *Cell,* November 2007)

2007 Nobel Prize in Medicine

Mario R. Capecchi, **Martin J. Evans** and **Oliver Smithies** for their discoveries of the principles for introducing specific gene modifications in mice by the use of embryonic stem cells.

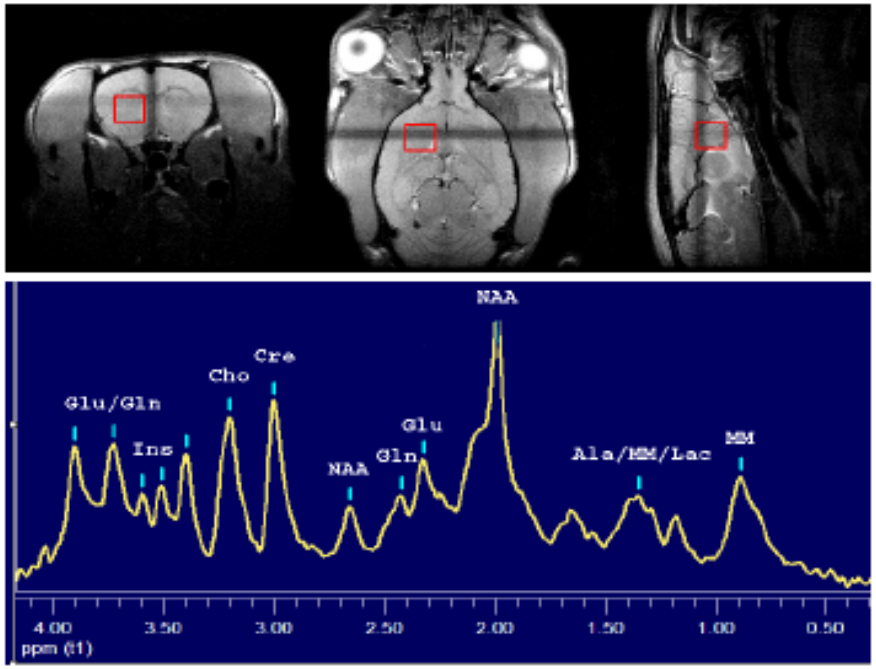
Tracking biomarkers for stem cells in the brain using magnetic resonance techniques

Using proton nuclear magnetic resonance spectroscopy, a specific BIOMARKER for neural stem and progenitor cells in the brain has been identified. The findings open avenues for investigating the role of neural stem cells and neurogenesis in a host of human brain disorders.

MR Spectroscopy Quantifying Brain Chemistry

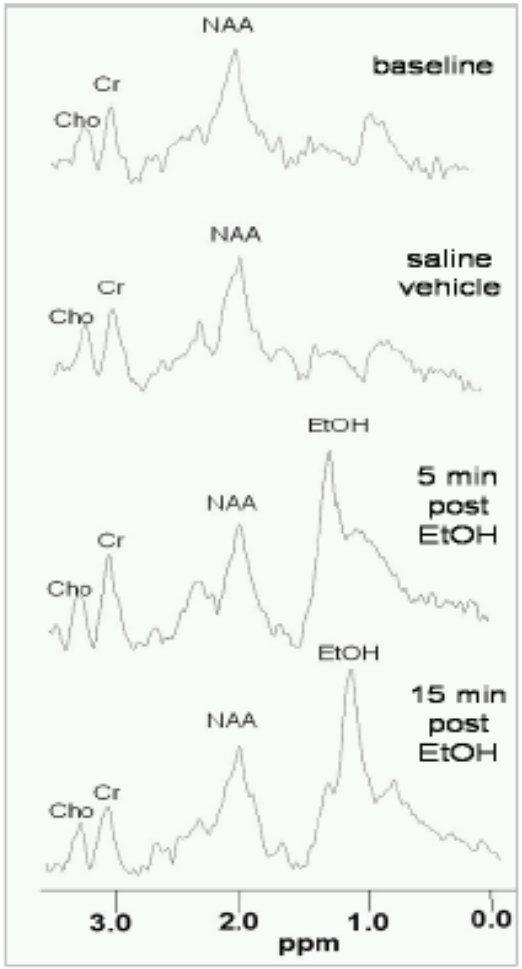
Applications

- phenotyping transgenic mice
- developmental biology
- neurotoxicology

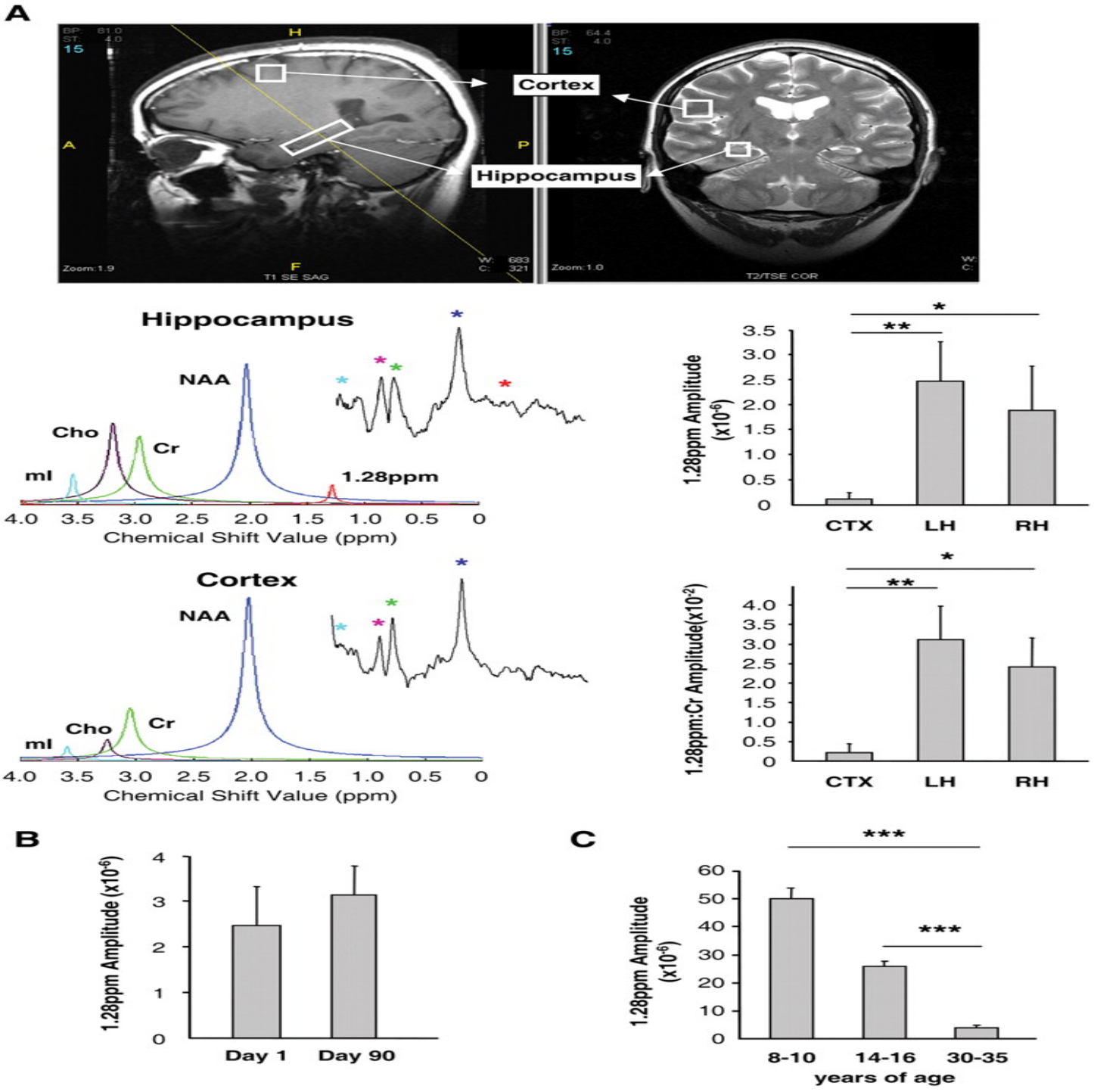


unpublished data, CCNI 4.7T

Brain EtOH Levels

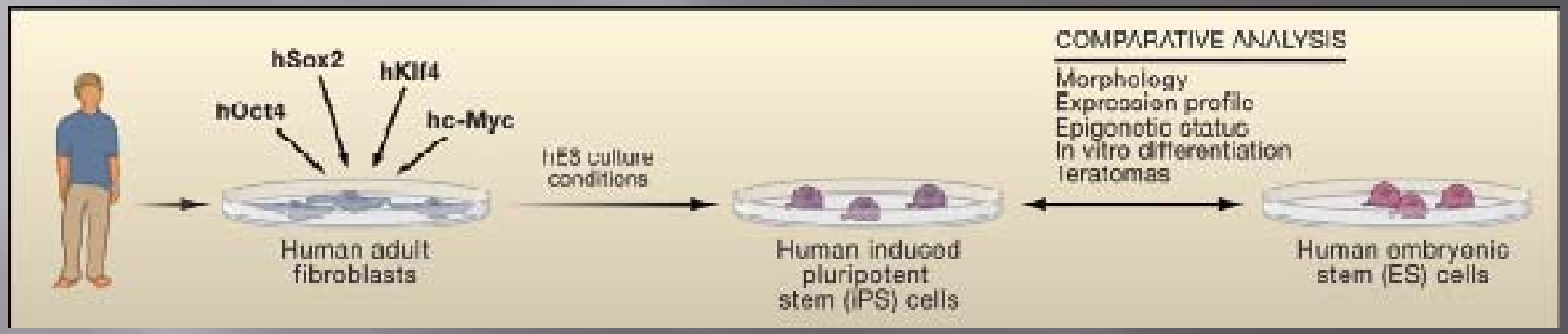


From Dr. Craig Ferris' lecture on Functional Magnetic Resonance Imaging



From Manganas et al., 2007. *Science* **318**: 980-985.

"Scientists Turn Human Skin Cells into Stem Cells"



Induction of Pluripotency: From Mouse to Human

Holm Zaehres[1] and Hans R. Schöler[1,*]
[1]Max Planck Institute for Molecular Biomedicine, Department of Cell and Developmental Biology, Münster, NRW 48149, Germany
*Correspondence: schoeler@mpi-muenster.mpg.de
DOI 10.1016/j.cell.2007.11.020

Please cite this article in press as: Takahashi et al., Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors, Cell (2007), doi:10.1016/j.cell.2007.11.019

Published Online November 20, 2007
Science DOI: 10.1126/science.1151526

Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors

Kazutoshi Takahashi,[1] Koji Tanabe,[1] Mari Ohnuki,[1] Megumi Narita,[1,2] Tomoko Ichisaka,[1,2] Kiichiro Tomoda,[3] and Shinya Yamanaka[1,2,3,4,*]
[1]Department of Stem Cell Biology, Institute for Frontier Medical Sciences, Kyoto University, Kyoto 606-8507, Japan
[2]CREST, Japan Science and Technology Agency, Kawaguchi 332-0012, Japan
[3]Gladstone Institute of Cardiovascular Disease, San Francisco, CA 94158, USA
[4]Institute for Integrated Cell-Material Sciences, Kyoto University, Kyoto 606-8507, Japan
*Correspondence: yamanaka@frontier.kyoto-u.ac.jp
DOI 10.1016/j.cell.2007.11.019

Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells

Junying Yu [1*], Maxim A. Vodyanik [2], Kim Smuga-Otto [1], Jessica Antosiewicz-Bourget [1], Jennifer L Frane [3], Shulan Tian [4], Jeff Nie [4], Gudrun A. Jonsdottir [4], Victor Ruotti [4], Ron Stewart [4], Igor I. Slukvin [5], James A. Thomson [6*]

Genes that encode the relevant factors were introduced into cells using retroviral vectors

Discussion:

Note that cells are pluripotent (capable of producing many cells types) and not totipotent (like ES cells); cells are referred to as "induced pluripotent stem (iPS) cells "

Note that a significant number of mice derived from iPS cells develop tumors because of the reactivation of an oncogene carried on the retroviral vector. Mice derived from ES cells are normal.

IMPACT :

Possibility of generating patient-specific stem cell lines to study the mechanism of different diseases in the laboratory

Creation of models for drug discovery and testing the toxic effects of drugs

Does this alter the debate about the use of human ES cells or not?

Acknowledgments

Lehigh Faculty participants:

Drs. Michael Burger, Neal Simon, Jennifer Swann, Jill Schneider, Lynne Cassimeris, Dimitrios Vavylonis, Samir Ghadiali, Linda Lowe-Krentz, Robin Dillon, Elizabeth Dolan, Jeffrey Sands, Daniel Lopresti, Jutta Marzillier, Stefan Maas, Ned Heindel, Vassie Ware

Guest speakers:

Drs. Craig Ferris (Northeastern University, John Glod,(University of Dentistry and Medicine, Robert Wood Johnson Hospital), Kimberly Wicklund, Mr. Mark Clymer (Olympus America)

American Society for Cell Biology:

iBioseminars from Drs. Ronald Vale, David Baltimore, Elaine Fuchs, Stanley Falkow, Lucy Shapiro

Funded by: Howard Hughes Medical Institute

THANK YOU!