2007 ANNUAL CIRM SCHOLARS MEETING

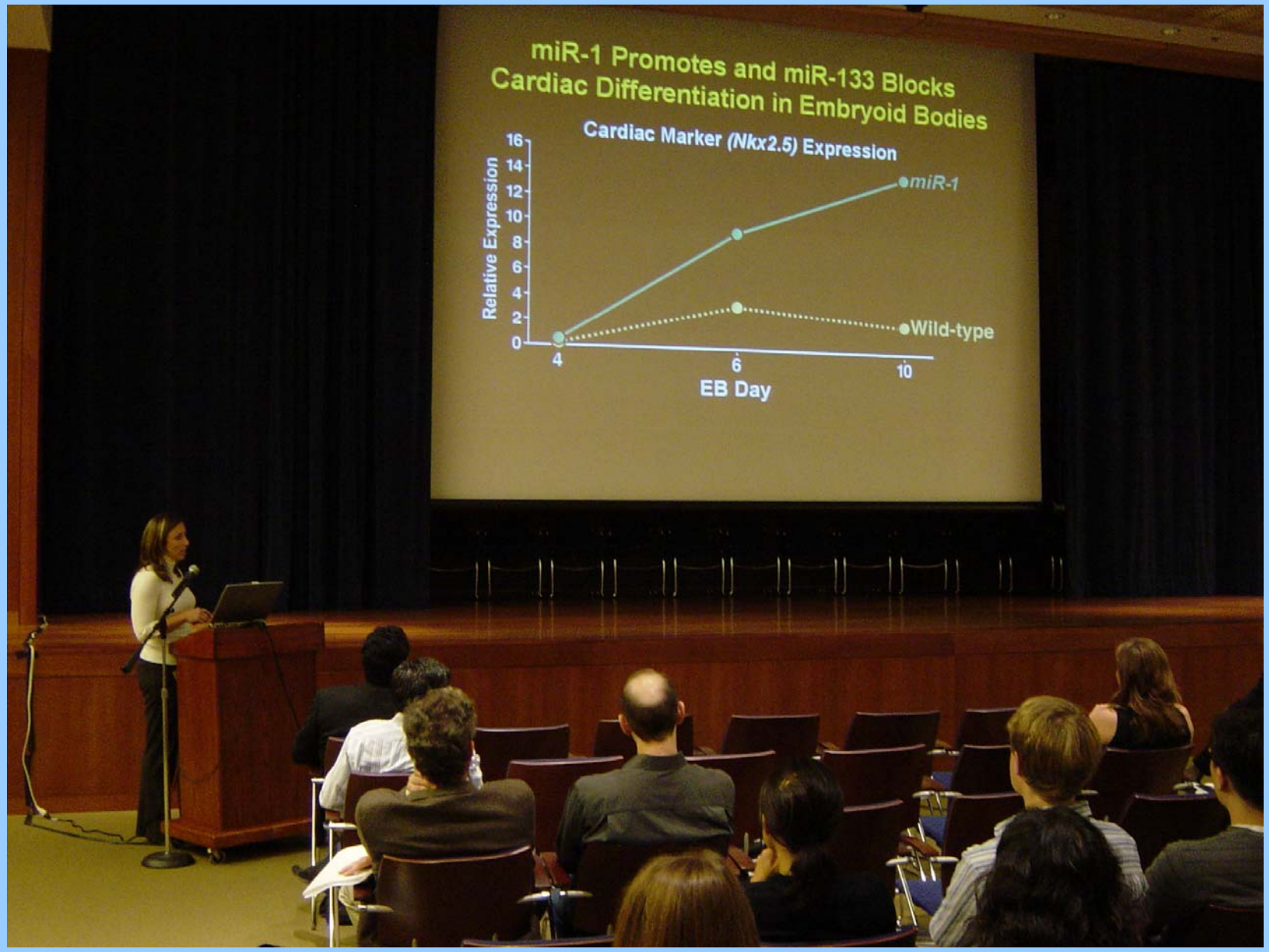
CALIFORNIA INSTITUTE FOR

CIRM

REGENERATIVE MEDICINE

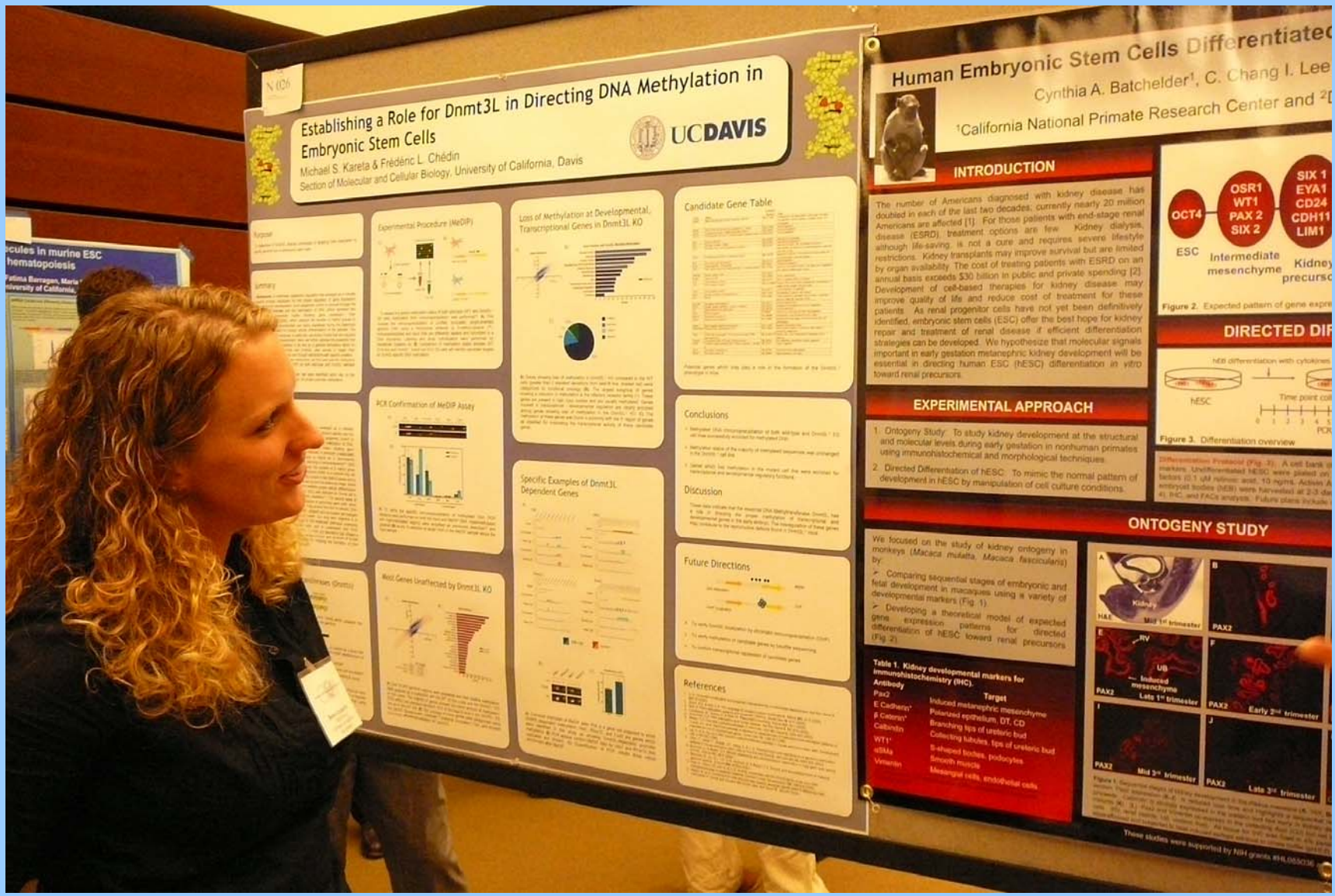
Meetings

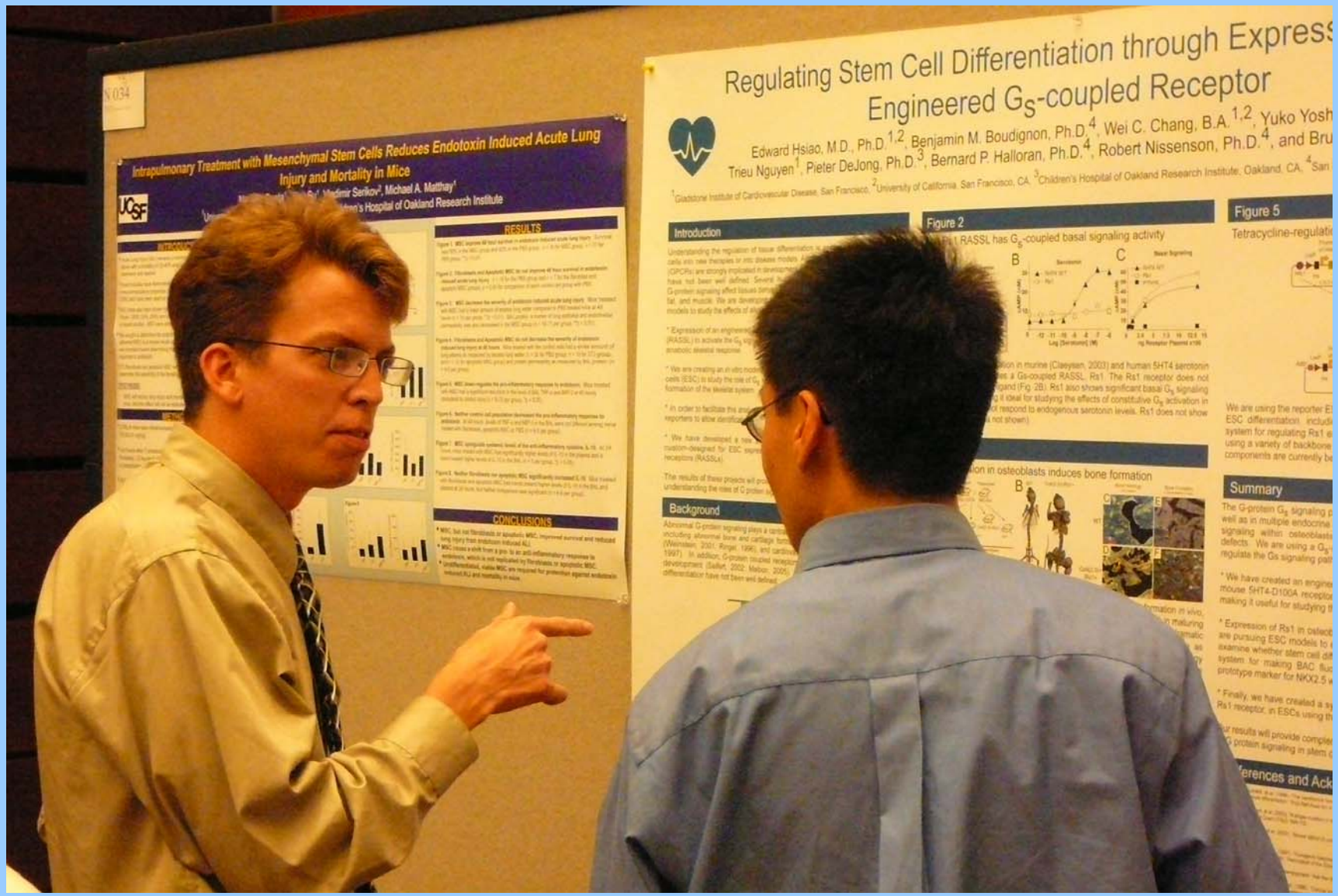
- Northern California Training Programs
  - Tuesday, September 11, 2007
  - UC San Francisco Mission Bay Campus
- Southern California Training Programs
  - Friday, September 28, 2007
  - UC Irvine Campus


miR-1 Promotes and miR-133 Blocks
Cardiac Differentiation in Embryoid Bodies
Cardiac Marker (Nkx2.5) Expression
Relative Expression
16
14
12
10
8
6
4
2
0
miR-1
Wild-type
4
6
10
EB Day


Notch Signaling Pathway
Jagged
Delta
Notch
Notch IC
EXIT


Cell in Acute Promyelocytic Leukemia is Mature Cell
Galit Rosen MD, Scott Kogan, MD. University of California, San Francisco
Progenitors are infrequent in acute promyelocytic leukemia
Progenitor FACS analysis of normal vs. leukemia cells. (A) FVB/N control bone marrow showing presence of HSC and myeloid progenitors (MP). (B) Leukemic spleen sample showing paucity of all hematopoietic progenitors.
LSC are lymph erythroid cKit+ Gr1+
Survival curve of mice transplanted with fractionated cells from leukemic spleens. The cKit+Gr1+ myeloblast population (blasts) is enriched for LSC; these mice have decreased survival compared to mice injected with whole unsorted leukemia. Fractionated cells that have variable expression of cKit but lack Gr1 (MP are within this gate) are not enriched for LSC: mice injected with these cells have similar survival to negative controls injected with lymphocytes.
Conclusion
Acknowledgements


Establishing a Role for Dnmt3L in Directing DNA Methylation in Embryonic Stem Cells
UCDAVIS
Michael S. Kareta & Frédéric L. Chédin
Section of Molecular and Cellular Biology, University of California, Davis
Purpose
Summary
Experimental Procedure (MeDIP)
PCR Confirmation of MeDIP Assay
Most Genes Unaffected by Dnmt3L KO
Loss of Methylation at Developmental, Transcriptional Genes in Dnmt3L KO
Specific Examples of Dnmt3L Dependent Genes
Candidate Gene Table
Conclusions
Discussion
Future Directions
References
Human Embryonic Stem Cells Differentiated
Cynthia A. Batchelder[1], C. Chang I. Lee
[1]California National Primate Research Center and
INTRODUCTION
The number of Americans diagnosed with kidney disease has doubled in each of the last two decades; currently nearly 20 million Americans are affected [1]. For those patients with end-stage renal disease (ESRD), treatment options are few. Kidney dialysis, although life-saving, is not a cure and requires severe lifestyle restrictions. Kidney transplants may improve survival but are limited by organ availability. The cost of treating patients with ESRD on an annual basis exceeds $30 billion in public and private spending [2]. Development of cell-based therapies for kidney disease may improve quality of life and reduce cost of treatment for these patients. As renal progenitor cells have not yet been definitively identified, embryonic stem cells (ESC) offer the best hope for kidney repair and treatment of renal disease if efficient differentiation strategies can be developed. We hypothesize that molecular signals important in early gestation metanephric kidney development will be essential in directing human ESC (hESC) differentiation in vitro toward renal precursors.
EXPERIMENTAL APPROACH
1. Ontogeny Study: To study kidney development at the structural and molecular levels during early gestation in nonhuman primates using immunohistochemical and morphological techniques.
2. Directed Differentiation of hESC: To mimic the normal pattern of development in hESC by manipulation of cell culture conditions.
OCT4
OSR1 WT1 PAX 2 SIX 2
SIX 1 EYA1 CD24 CDH11 LIM1
ESC
Intermediate mesenchyme
Kidney precurso
Figure 2. Expected pattern of gene expre
DIRECTED DI
NEB differentiation with cytokines
hESC
Time point col
Figure 3. Differentiation overview
ONTOGENY STUDY
We focused on the study of kidney ontogeny in monkeys (Macaca mulatta, Macaca fascicularis) by:
Comparing sequential stages of embryonic and fetal development in macaques using a variety of developmental markers (Fig. 1).
Developing a theoretical model of expected gene expression patterns for directed differentiation of hESC toward renal precursors (Fig. 2).
Table 1. Kidney developmental markers for immunohistochemistry (IHC).
Antibody | Target
Pax2 | Induced metanephric mesenchyme
E Cadherin* | Polarized epithelium, DT, CD
β Catenin* | Branching tips of ureteric bud
Calbindin | Collecting tubules, tips of ureteric bud
WT1* | S-shaped bodies, podocytes
αSMa | Smooth muscle
Vimentin | Mesangial cells, endothelial cells
Kidney
H&E
Mid 1st trimester
PAX2
RV
UB
Induced mesenchyme
Late 1st trimester
Early 2nd trimester
Mid 3rd trimester
Late 3rd trimester
These studies were supported by NIH grants #HL055036


Intrapulmonary Treatment with Mesenchymal Stem Cells Reduces Endotoxin Induced Acute Lung Injury and Mortality in Mice
UCSF
RESULTS
CONCLUSIONS
Regulating Stem Cell Differentiation through Express
Engineered G_S-coupled Receptor
Introduction
Figure 2
Figure 5
Tetracycline-regulati
Background
Summary


EXIT


EXIT

protocols.

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