CLL Sample
(N = 5,300)

**Immunophenotyping**
Surface & intracellular

**Clinical Trials**
Accrual, tracking, correlative studies

**Clinical data**
WBC, Rai, Dx, Tx

**Serial samples**
Longitudinal studies

**DNA & RNA**
Molecular studies

**Plasma/Serum**
ELISAs

**Blood smears**
Immunohistochemistry

**Demographic**
Age, sex, race

**Cytogenetics**
FISH karyotype

**Cellular Kinetics**
B-cell turnover rates CD38/Ki67/CXCR4

**Buccal swabbs**
Germline DNA Genetics studies

**ZAP-70/CD38**
prognosis

**IGHV**
Mutational status prognosis

**Clinical Trials**
Accrual, tracking, correlative studies

**Clinical data**
WBC, Rai, Dx, Tx

**Serial samples**
Longitudinal studies

**DNA & RNA**
Molecular studies

**Plasma/Serum**
ELISAs

**Blood smears**
Immunohistochemistry

**Demographic**
Age, sex, race
Tissue Core facilitates and expedites CRC discoveries?

1) Immunophenotyping: ZAP studies, others markers: Ki67, CXCR4, TCL-1

2) IGHV mutation status: VH studies

3) Cytogenetics: QA/QC, Cyto studies

4) Clinical: data entry, QA/QC CRC Clinical trials

5) CRC Clinical trials: facilitate correlative science

6) Serial samples: Longitudinal studies, disease evolution
## CRC Immunophenotyping Panel 2011

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Tissue Core-Biorepository Serial samples acquisition

2100/5300 (40%) pts in CRC have serial samples
*N=200 to *N=2100 ------>10 fold increase serial sample accrual
A = pt has non-progressive disease & stable WBC over time

B = pt has exponential increase in WBC over time

C = pt has an acceleration in the kinetics of the leukemia cell doubling time

Merit: Longitudinal studies

Acquisition of serial samples enables studies on the different kinetics in the increase of WBC over time. Review of the clinical data on all these cases characterized by serial samples, will allow the CRC investigators to segregate cases that have indolent & non-progressive disease from those who have a change in the kinetics of disease progression (core A & B).
A pts = serial smpls : at least 3 smpls & clinical data on at least 2 smpls
B pts = serial smpls : at least 2 smpls & clinical data on at least 1 smpl
C pst = one sample : 1 & clinical data on 1 smpl
D pts = one sample : clinical data not yet present
Tissue Core - FISH studies

Cytogenetics Team

CRC Cytogenetics Lab Directors:
- Daniel Van Dyke, Mayo Clinic
- Nyla Heerema, Ohio State University
- Paola Dal Cin, Brigham and Women's Hospital (DF)
- Marie Dell'Aquila, UC San Diego
- Ayala Aviram, Long Island Jewish

CRC Coordinators/Interactions:
- Laura Rassenti, Coordinate (UCSD) --- studies/data updates
- Andrew Greaves, Data (UCSD) --- input/storage/output
- Donna Neuberg, Biostats (DF) --- oversee data/studies design
- Jeanette Eckel-Passow, Biostats Mayo --- QA/QC data (SAS)
- Carlo Croce, Project 1 (OSU) --- use of data/collaborations

All CRC PIs for Clinical data updates, FISH data --- mining/studies

*** Monthly teleconferences
*** CRC FISH website (all updates) https://cllresearch3.ucsd.edu/
Role of CRC Cytogeneticists

1) Oversee FISH & karyotype uniform data entry from CRC Sites
   Data entered for each sample with blood in the Tissue Core:
   close to DX, serials, before 1st Tx

2) Assure QA/QC of all FISH Data for data retrieval by CRC
   Mayo: Jeanette Eckel Passow
   DF: Donna

3) Individual Cytogeneticist Hypothesis-driven study
Tissue Core
Cytogeneticists accomplishments:
2 publications


Standarized FISH scoring, data entry, & retrieval

*Dec 1, 05 = 15% of CRC pts had FISH data
*Dec 1, 10 = 62% of CRC pts have FISH data
1) **Cellular Kinetics**: use of Tissue Core immunophenotyping data

   A) Surface 4-color-Immunophenotyping: to date CLLs characterized \( N = 4,600 \) (90%)

   B) Intracellular immunophenotyping: to date CLLs characterized \( N = 4,600 \) (90%)
   - ZAP-70, TCL1, Ki67
   - All data analyzed by Flow-Jo software & entered in the CRC database
   - Correlations with prognostic markers/serial samples/longitudinal studies

2) **IGHV studies**: use of Tissue Core IGHV mutational status data

   - IGHV mutation status: to date CLLs characterized \( N = 3,300 \) (65%)
   - All sequence data analyzed by: IMGT/V-Quest: [http://imgt.cines.fr/IMGT_vquest](http://imgt.cines.fr/IMGT_vquest)
   - All data uniformly entered & retrieved

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All Interactions with informatics & biostatistics (Cores A & B)
Tissue Core-Biorepository
Role to facilitate CRC Clinical trials
(according to the specifics of each CRC protocol)

Tissue Core has organized:
Samples acquisition: collection kits
Sample storage: track time points
Participated nurses teleconferences
Tracking: forms database entry
Sample analysis analysis: Flow, ZAP, VH
Sample distribution for correlative studies

CRC Protocols
CRC002: Campath
CRC004: HDMP Ritux
CRC005: Campath SubQ
CRC008: GM-CSF
CRC0011: Heavy Water
CRC0012: OFAR2
CRC0014: Revlimid

Collaborations:
Core A, B, D
All CRC Projects: Correlatives studies
Tissue Core-Biorepository

1) Surface Immunophenotyping
   CD5/CD19/Kappa/Lambda/CD3/CD23
   CD20/CD38
   ROR1/CXCR4

2) Intracellular immunophenotyping
   ZAP-70
   TCL1
   Ki67

3) IgVH mutation status

Use of acquired data:
Cores A,B,D
All Projects
Chiorazzi/Kipps:
   VH studies, CLL antigens
   B cell proliferation compartment
Croce: TCL1 studies
Kipps: role ROR1, NLC
Kay/Burger: NLC - stroma
Byrd: methylation

Merit:
1) Prognosis/Therapy
2) Clinical Trials:
   Correlative sciences
   Response to Tx
3) Longitudinal studies/Disease
   Evolution
4) Stability of markers over time
The Tissue Core acquires SERIAL samples during the disease progression of the CLL patients that are registered in the CRC.

The serial samples of from the CLL patients are characterized according to their surface antigen phenotype by multiparameter flow cytometric analysis and clinical information.

This enables the CRC investigators to examine for longitudinal changes in the leukemia cell’s genotype, biochemistry, and/or immunologic phenotype and correlate these data to clinical outcome.
1) INCREASE accrual of SERIAL samples and corresponding clinical data

2) Immunophenotyping:
   as requested for
   Specific Hypothesis-Driven studies
   & CRC Clinical Protocols

**Use of acquired data:**
- Cores A,B,D
- All Projects
- Chiorazzi/Kipps:
  - B cell proliferation compartment
- Croce: TCL1/miRNA serial studies
- Kipps: role ROR1, NLC
- Kay/Burger: NLC - stroma
- Byrd: methylation

**Merit:**
1) Prognosis/Therapy
2) Clinical Trials:
   - Correlative sciences
   - Response to Tx
3) Longitudinal studies /Disease Evolution
4) Stability of markers over time

**Surface:**
CD5/CD19/Kappa/Lambda
CD3/CD23
CD20/CD38
ROR1/CXCR4

**Intracellular:**
ZAP-70
TCL1
Ki67
Collection Schema

Sample Collection:
- Blood (1,2,3,4)
- Buccal swabb (1)
- Plasma (1,2,3,4)
- Serum (1,2,3,4)
- Slides (1,2,3,4)
- Familial CLL smpls

Use of Data:
- Cores A,B,D
- All Projects

Merit of continued accrual:
1) Prognosis/Therapy
2) Correlative science
3) Longitudinal studies
4) Increase probability to capture pts with unique mutations (P1)

Tissue Core: Monthly Updates of Samples Acquired & Distributed to all CRC members
emails & Website: https://cllresearch3.ucsd.edu/
Chateau Lafite Rothschild - (yr 1959 @ $2,200/bottle)

The CRC Tissue Core:
Is getting better with time

Thanks to all CRC members!
Thanks to all

CRC Meeting ASH 2010