Kevin Cullen, MD, Director, University of Maryland Greenebaum Cancer Center and Professor, University of Maryland School of Medicine
UMGCC – Who are we and why are we here?

The mission of the UMGCC is to undertake innovative basic and clinical research that will impact the understanding and treatment of cancer around the world and to provide state-of-the-art clinical care to cancer patients in Maryland and beyond.
UMGCC at a Glance (2015)

- 2600 New Cancer patients/year
- >60,000 Outpatient Visits, >2000 inpatient admissions
- 5 Research Programs, 7 core laboratories
- 257 faculty members (113 full, 141 assoc) including:
  - 4/11 USM Universities
  - 4/6 UMB Schools
  - 14/25 UMSOM Departments
- NCI Total Funding $18.1M
- Total Cancer Research Funding $56.7M
- 188 Clinical Trials (684pts total)
Programs and Shared Services

2013
- Hormone Responsive Cancers
- Molecular & Structural Biology
- Experimental Therapeutics
- Viral Oncology
- Tumor Immunology and Immunotherapy

2015
- Hormone Responsive Cancers
- Molecular & Structural Biology
- Population Science
- Experimental Therapeutics
- Tumor Immunology and Immunotherapy

NCI-CC
A Cancer Center Designated by the National Cancer Institute

University of Maryland Marlene and Stewart Greenebaum Cancer Center
NCI Cancer Center Support Grant (P30) Renewal – *requests elevation to Comprehensive Cancer Center*
Research Highlights
Scientific Accomplishments

- Drs. Vincent Njar and Angela Brodie invent galeterone for the treatment of advanced prostate cancer
- 6/24/15 ARMOR3-SV, Tokai’s pivotal Phase 3 clinical trial of galeterone in men with metastatic castration-resistant prostate cancer (mCRPC) whose tumors express the AR-V7 splice variant, which is a truncated form of the androgen receptor (AR) that has been associated with non-responsiveness to commonly-used oral therapies for mCRPC.
Qiu - Discovered novel AR variants that underlie castration resistant prostate cancer

Collaborations: NYU; NCI; UCLA; UC-Davis
Funding: RO1 CA106504; RO1 CA169524
Shared Services: GSS, FCSS
Brodie, Njar - Galeterone inhibits AR and AR variants in treatment naïve and castration-resistant prostate cancer

Invented novel synthesis inhibitor galeterone that also downregulates AR:

VN124 - preclinical UMGCC

- Tokai licensed Galeterone
- Fast Track for CRPC Phase I, II, III

Patients with AR c-terminal loss

ARMOR3-SV ARv7, mCRPC Precision Medicine

Funding: RO1 CA129379, VA Merit, RO1 CA027440


Shared Services: BSS, GSS
Investigational device exemption from FDA; Clinical trial to begin late 2015 (UMGCC, UTSW, KU, Allegheny, Ottawa)
Reduced radiation to heart, lungs
Quality of Life - our catchment area; ablative therapy in 1 day versus 10-11 weeks

Funding: R44 CA132254
Recent Progress – Theme 3

AEOL 10150 for mitigation of lung radiation injury – Zeljko Vujaskovic, Isabel Lauren Jackson, Thomas MacVittie

Preclinical drug development
Mitigation of radiation-induced pneumonitis/fibrosis in clinically relevant rodent models

Initiation of clinical trial in NSCLC patients (2015)
AEOL 10150 enhances NSCLC radiosensitivity
Reduces pneumonitis and steroid use in NHP exposed to WTI

Hadley et al. Int Con Rad Res 2011
Garofalo et al. Health Physics 2014

Shared Services
• Flow Cytometry
• Biostatistics

AEOL 10150

Graph: Tumor volume vs. Treatment

Graph: Percent survival vs. Days Post-WTLI

Bar Chart: Average Ratio of Clinical/Normal Cells

Histogram: Pneumonitis & Fibrosis

Histogram: Pulmonary Effusions

Histogram: Dexamethasone Support

Legend:
- AEOL 10150
- Control
- AEOL
- Rad
- Rad + AEOL

Legend:
- No Damage
- MNB
- Moderate-Bad

Legend:
- 28%
- 45%
- 33%
David Weber (MSB) & Frank McCormick (UCSF, FNL): “Targeting the KRAS4B oncogene and its complexes”

Funding: RAS initiative (CRADA: CBT, FNL, UCSF)

Growth factors → Ras-GDP

RTK → Ras-GDP

DAG → NMDA-R

NMDA → NMDA-R

Ras-GTP → Ras-GRP

GAPs: NF1-SPRED, p120 GAP

GEFs: Sos, RasGRP, RasGRF1

PLCε, TIAM-1, RASSF

RIN

AF6

IMP

RAP1

Grb7

PDZGEP

KIAA1849

RalGDS

RalA

RalB

Filamin

RalBP1

Exo84

Sec5

ZONAB

Erk

Mek

PTEN

PI3-Kinase

PIP3

PIPK1

S6 Kinase

4E-BP1

Mdm2

Cyclin D1, etc

RTK -> Ras-GTP

Mek -> Raf

KSR

PTEN

PI3-Kinase

PIP3

PIPK1

S6 Kinase

4E-BP1

Mdm2

Cyclin D1, etc

ERK1/2

RheB

mTORC1

S6 Kinase

4E-BP1

Stephen et al, Cancer Cell (2014)

Nussinov et al, Mol Canc Res (2015); PI3Kalpa-CaM-KRAS

http://www.cancer.gov/research/key-initiatives/ras/groups/structure-biophysics
P50 PI, Dr. Pamela Clark speaking on e-cigarettes to NCI Director and National Cancer Advisory Board

Who is Selling Them?

- About 200 makers
- Swallowing the independent market
  - Lorillard
  - Altria (Philip Morris)
  - RJ Reynolds
  - British American Tobacco
Community State Types (CST)
I – L. crispatus
II – L. gasseri
III – L. iners
IVA – Low Lactobacillus
IV-B – Low Lactobacillus
VI - Proteobacteria

Vaginal Microbiome & HPV Infection in Nigerian Women

![Graph showing the percentage of negative and positive HPV for each Community State Type (CST).]

Dareng, Epidemiol Infect 2015

Vaginal Microbiome & HPV Clearance Rate in Baltimore Women

![Graph showing the clearance rate of HPV in different CST types.]

Brotman, J Infect Dis 2014

Additional Microbiome Research

- Anal microbiome and HPV prevalence (PI: Nowak)
- Gut microbiome and estrogen metabolism (PI: Ravel)
- Gut microbiome and breast cancer risk (PI: Ravel)
- Oral microbiome and smoking (PI: Sapkota)
Leveraging NCI status to serve our community – the UMB CURE Scholars Program

- $750K supplement to NCI center grant funded by the NCI center to reduce health disparities

- Matches 43 west Baltimore middle school students with a team of mentors for 3x/week tutoring and mentoring in science and math – will continue through high school

- First NCI funded program in the US aimed at middle school students

- Will make scholars more competitive for undergraduate and graduate training in science and research
University of Maryland Cancer Network
## Cancer Program Size (New Patients) by Tumor Registry Count

<table>
<thead>
<tr>
<th>New Cancer Patients*</th>
<th>CY 2013</th>
<th>CY 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>UMGCC</td>
<td>2,590</td>
<td>2,645</td>
</tr>
<tr>
<td>UM BWMC</td>
<td>1,092</td>
<td>1,237</td>
</tr>
<tr>
<td>UM UCH</td>
<td>1,020</td>
<td>1,195</td>
</tr>
<tr>
<td>UM SJMC</td>
<td>1,087</td>
<td>1,080</td>
</tr>
<tr>
<td>UM SRH</td>
<td>1,192</td>
<td>991</td>
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<tr>
<td>UM CRMC</td>
<td>205</td>
<td>176</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>7,186</strong></td>
<td><strong>7,324</strong></td>
</tr>
</tbody>
</table>

1/3 of newly diagnosed cancer patients in Maryland are treated at a UMMS hospital

* 24,000 New Cancer Cases in Maryland Annually (Includes analytic and non analytic cases)
Gov. Hogan leaves the hospital after completing chemotherapy - Oct 13, 2015
Strategic Plan – the next 5 years

- Expand innovative basic and clinical research with CRF support
- Develop the University of Maryland Cancer Network to provide optimal, cost effective cancer care across the state
- Continue our mission of outreach to underserved populations throughout Maryland
- Continue our mission of training from middle school students all the way to clinical subspecialists
- Plan and launch a new home for the UMGCC