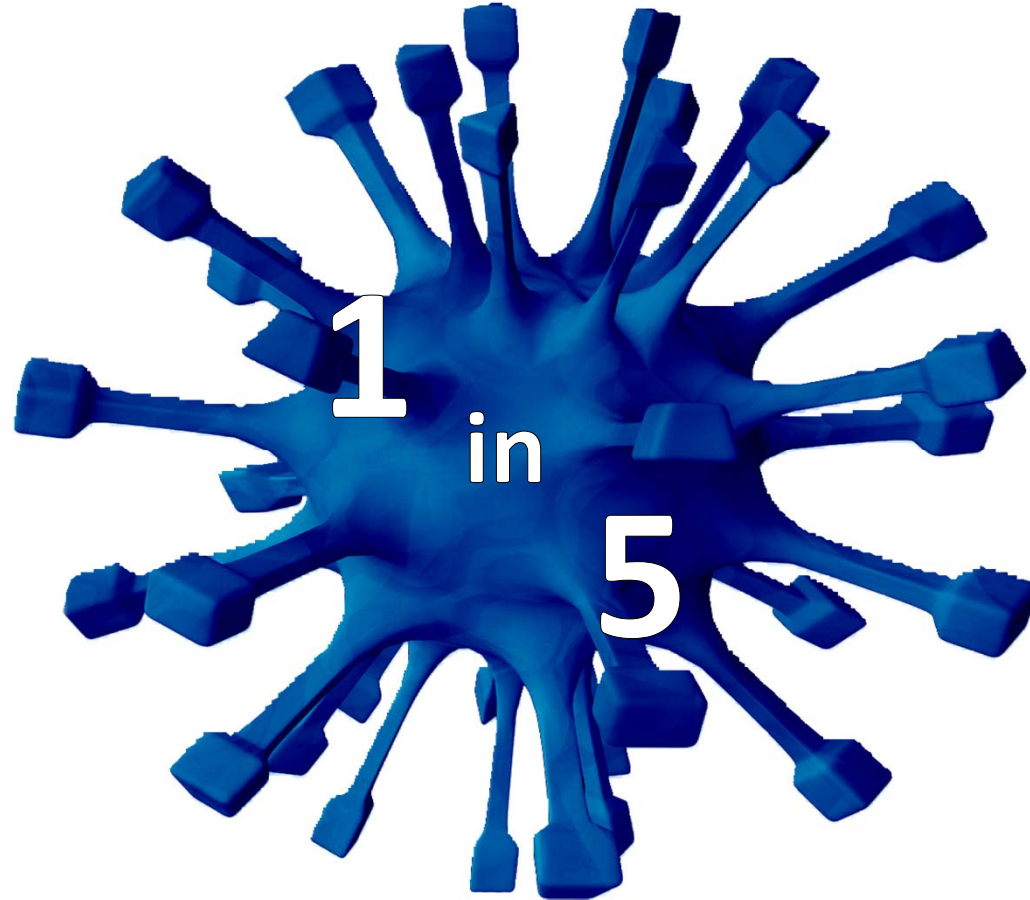


CENTER FOR  
INFECTION  
RESEARCH IN  
CANCER



**Anna R Giuliano, PhD**  
**Director**

# *Number of Cancers Caused by Infections\**



(\*That we know of)

# Examples of Tumor Types Known to be Caused by Infections

Tumor Type	Infectious Cause
Cervix; anal and perianal cancers (>90%)	Various HPV types
Vulvar, penile and vaginal cancers (~50%)	
Head and neck cancers (~78%)	
Squamous cell carcinomas of skin (unknown attributable fraction)	
Hepatocellular carcinomas	Hepatitis B and C viruses
B-cell lymphomas in immunocompromized patients (50%) and in some T-cell lymphomas	Epstein-Barr Virus
Burkitt's lymphoma	
Nasopharyngeal cancer	
Hodgkin's lymphoma (30-40%)	
Gastric cancer (10%)	
Adult T-cell leukemias	HTLV-1
Seminomas	Endogenous retroviruses
Kaposi's sarcoma	HHV-8
Gastric cancer and gastric lymphoma	<i>Helicobacter pylori</i>
Bladder cancer; rectal cancer	Schistosoma species
Cholangiocarcinoma	Opisthorchis species; <i>Clonorchis sinensis</i>

# *CIRC Goals*

## IDENTIFY

IDENTIFY new infectious agents and establish a causal link with cancer.

## DEVELOP

DEVELOP novel approaches for prevention, early detection, and treatment of cancers caused by infectious agents.

## TRANSLATE

TRANSLATE findings into new standards for personalized care with novel vaccines, lower dose radiotherapy, and new antiviral drugs.

## DISSEMINATE

DISSEMINATE and increase adoption of effective prevention and treatment interventions for infection-related cancers into clinical and public health practice.

# *CIRC's International Strategic Partners*



# CIRC Pilot Grants Funded

Grant	PI
<b>Funded 2013</b>	
<i>Developing a brief communication intervention for Family Medicine residents to overcome parental barriers to HPV vaccination</i>	Vadaparampil
<b>Funded 2014</b>	
<i>Role of cancer stem cells in the genesis of H. pylori related gastric cancer compared to H. pylori unrelated gastric cancer in Colombia and US populations</i>	Coppola
<i>Paving the road to molecular immunofluorescent anoscopic screening and surveillance: A pilot study</i>	Shibata/Siegel
<i>Cutaneous viral infections in non-melanoma skin cancers among chronic lymphoid leukemia patients</i>	Rollison
<i>The role of human herpesvirus 6 in the etiology of Hodgkin's lymphoma</i>	Sokol/Medveczky
<i>An infectious etiology of ovarian cancer: A pilot study</i>	Robertson

# Ovarian Cancer Pilot Project (Robertson)

## Overall Survival

Virus of interest versus no virus of interest

log-rank test:  $p = 0.0003$

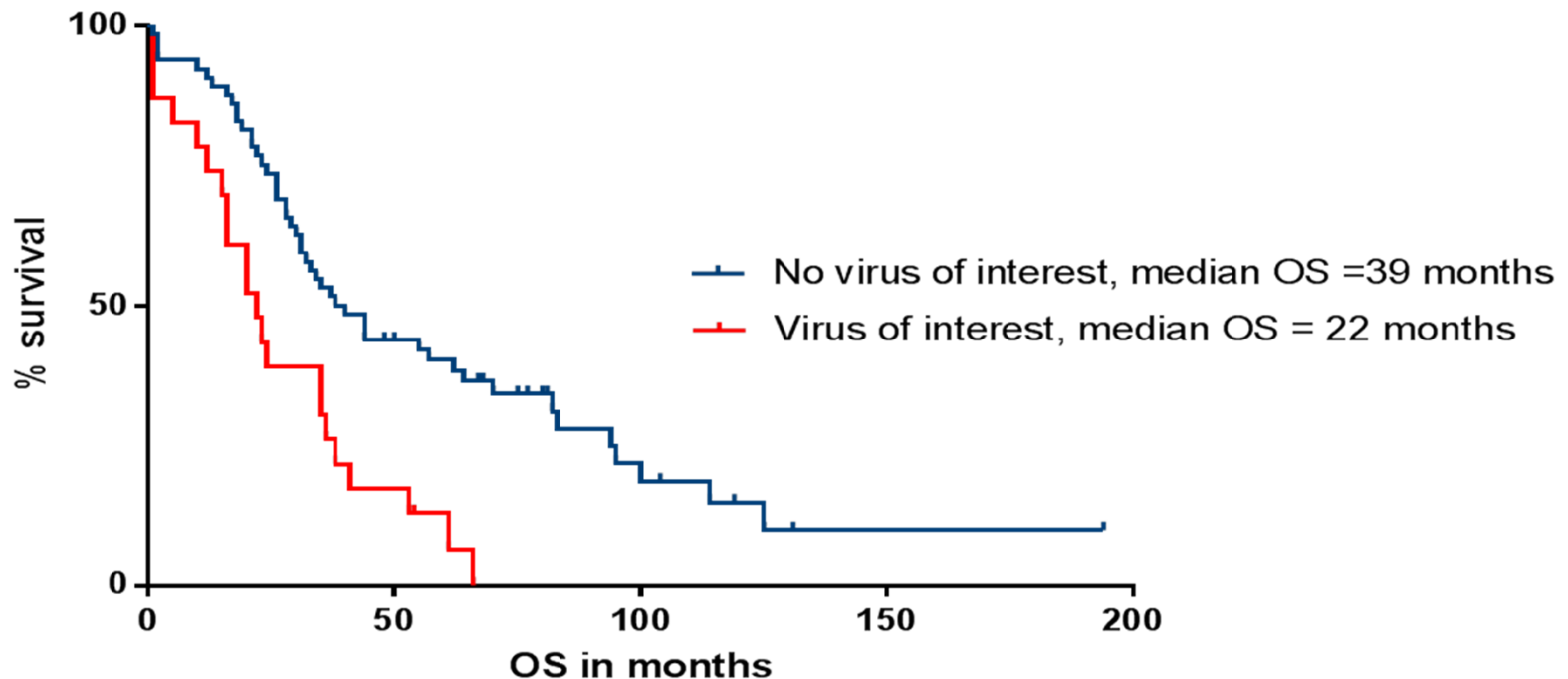
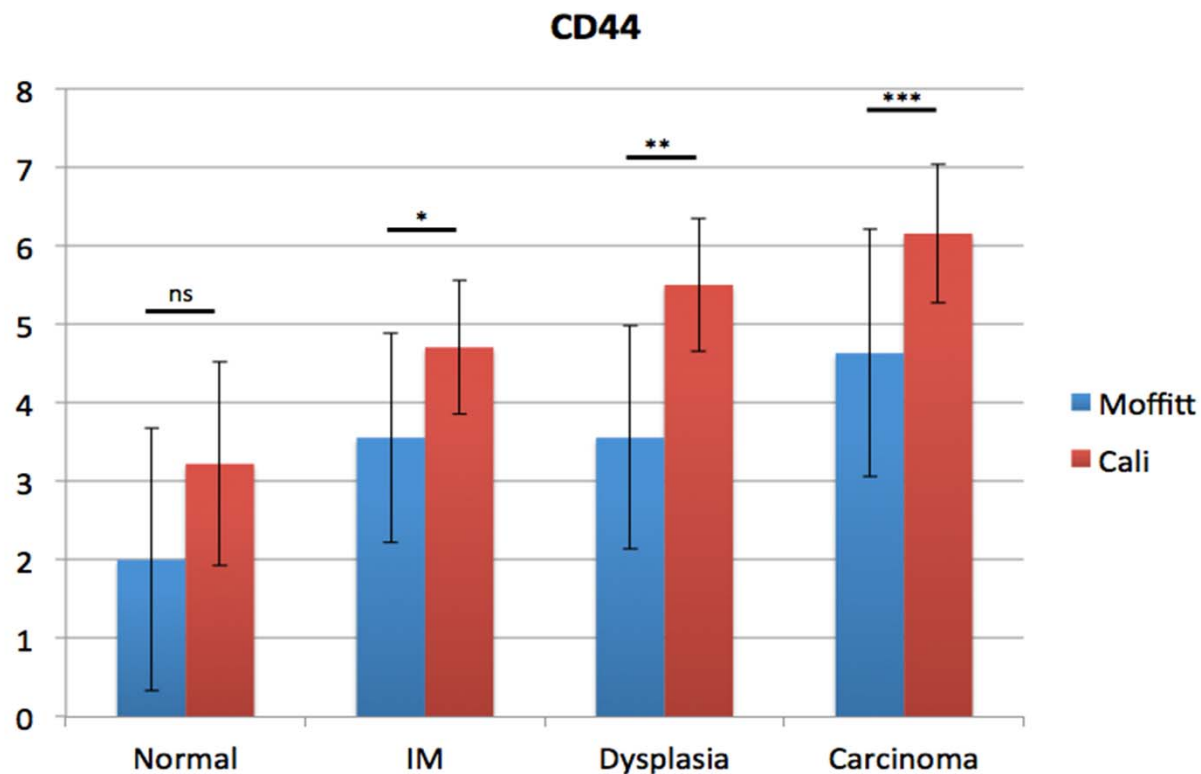


Figure 1: Comparison of overall survival for total  $n=87$  samples. Samples containing a virus of interest had a median overall survival of 22 months versus samples with no virus of interest which had an overall survival of 39 months. This difference was statistically significant ( $p=0.0003$ ).

# H. Pylori Pilot Project (Coppola)

Despite the well established link between gastric cancer and H. pylori infection, a screening program for early gastric cancer detection does not exist

**Aim:** Assess variation in gastric stem cell populations along gastric cancer continuum – potential screening biomarker?





# *IMO Viruses in Cancer Workshop*

## *November 2014*

- Large teams of faculty and staff from multiple divisions
- One project selected for funding, but members of each team continue to interact and are acquiring further pilot data and writing grant submissions



- ***H. Pylori*** – awarded IMO pilot funding
- **Microbiome** – Team Science grant awarded
- **HCV** – NIH application in preparation
- **HPV** (penile) – pilot project underway to gather preliminary data

# Vaccination Success to Date: The HPV Story

All girls and women ages  
9 to 26 years of age  
should be vaccinated with  
a three dose series of Gardasil™



**GARDASIL.**  
[Human Papillomavirus Quadrivalent  
(Types 6, 11, 16, and 18) Vaccine, Recombinant]

Your **SON** or **DAUGHTER** could be **oneless**  
person affected by HPV disease.

▶ **PARENTS:**  
Why GARDASIL for your son or daughter?  
[Find Out](#)



  
**KEEP  
CALM**  
we will have  
**Gardasil 9**



## The NEW ENGLAND JOURNAL of MEDICINE

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Efficacy of Quadrivalent HPV Vaccine against HPV Infection and Disease in Males

Anna R. Giuliano, Ph.D., Joel M. Palefsky, M.D., Stephen Goldstone, M.D., Edson D. Moreira, Jr., M.D.,  
Mary E. Penny, M.D., Carlos Aranda, M.D., Eftyhia Vardas, M.D., Harald Moi, M.D., Heiko Jessen, M.D.,  
Richard Hillman, M.D., Yen-Hwa Chang, M.D., Daron Ferris, M.D., Danielle Rouleau, M.D.,  
Janine Bryan, Ph.D., J. Brooke Marshall, Ph.D., Scott Vuocolo, Ph.D., Eliav Barr, M.D.,  
David Radley, M.S., Richard M. Haupt, M.D., and Dalya Guris, M.D.

### A 9-Valent HPV Vaccine against Infection and Intraepithelial Neoplasia in Women

E.A. Joura, A.R. Giuliano, O.-E. Iversen, C. Bouchard, C. Mao, J. Mehlsen,  
E.D. Moreira, Jr., Y. Ngan, L.K. Petersen, E. Lazcano-Ponce, P. Pitisuttithum,  
J.A. Restrepo, G. Stuart, L. Woelber, Y.C. Yang, J. Cuzick, S.M. Garland, W. Huh,  
S.K. Kjaer, O.M. Bautista, I.S.F. Chan, J. Chen, R. Gesser, E. Moeller, M. Ritter,  
S. Vuocolo, and A. Luxembourg, for the Broad Spectrum HPV Vaccine Study\*

# *HPV Vaccine UF-Moffitt Collaborations*

- **Cervical Cancer Prevention Among Low Income Adolescents in Florida**
  - Vadaparampil, Giuliano (Moffitt), Staras, Shenkman (UF)
  - UF/Moffitt Collaborative Initiative
  - Association between parental HPV knowledge, attitudes, and perceived vaccine accessibility and receipt of HPV vaccine
  - 5 peer reviewed publications
- **Health Technology Intervention to Increase HPV Vaccine Series Initiation**
  - Staras, Livingston, Thompson, Shenkman (UF), Vadaparampil (Moffitt)
  - Society of Adolescent Health and Medicine (SAHM)
  - Develop an intervention to increase HPV vaccine initiation among low income adolescents
  - 2 peer reviewed publications

# *Local HPV Vaccine Meeting*

- PITCH (Partnership to Immunize Teens and Children against HPV) was one of 18 supplements awarded to NCI Cancer Centers
- Led by CIRC Investigators Dr. Anna Giuliano and Dr. Susan Vadaparampil

- January 14, 2015  
First meeting of PITCH Stakeholders to discuss strategies to increase HPV vaccination in FL





# *Cervical Cancer Free Coalition (CCFC) Florida*

## *U Miami- Moffitt Collaboration*

Kobetz (U Miami), Vadaparampil (Moffitt)

- Identify key stakeholders necessary to reduce the burden of cervical cancer in Florida
- Engage stakeholders in the development of a statewide network reduce the burden of cervical cancer in Florida
- Create a state level agenda to reduce incidence, morbidity, and mortality of cervical cancer in Florida thorough sustained collaboration



# *National HPV Vaccine Meeting*

## **Increasing HPV Vaccination in the U.S.: A Collaboration of NCI-funded Cancer Centers**

- Discussion of national strategy, common goals and approaches - led by CIRC
- 76 representatives from 37 cancer centers
- Top-level representatives from the NCI, CDC, ACS, and U.S. Congress



**CIRC**

*Future Directions*

# *Training the Next Generation of Scientists*

## *K05 Senior Mentor Award*

- *2014-2015* - 5 trainees and co-Mentors from:
  - Health Outcomes and Behavior
  - Cancer Epidemiology
  - GYN Oncology
  - Infectious Diseases
- *2015-2016* – 8 trainees and co-Mentors from:
  - IMO
  - Cancer Epidemiology
  - Radiation Oncology
  - GU Oncology
  - Pathology
  - Immunology



# *CIRC Retreat 2015*

## *Provocative Questions*

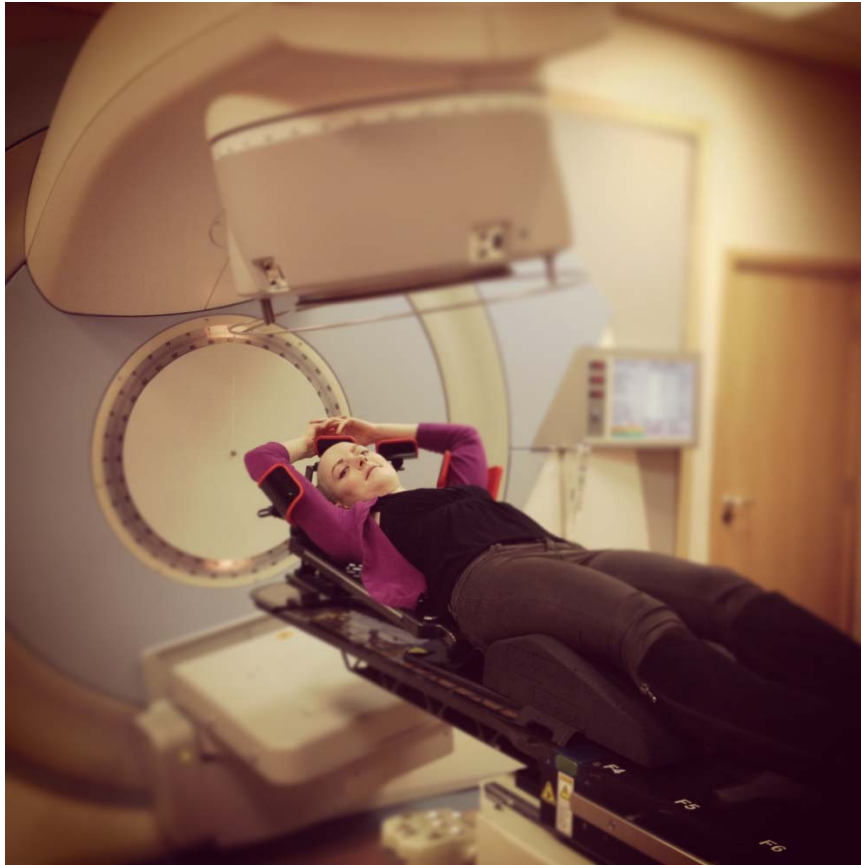
**Why do only a minority of individuals with infections progress to cancer?**

**Why are cancers caused by infection highly sensitive to radiotherapy?**

**Do cancers caused by infections have increased immune activation?**

**Where we have had success (e.g., HPV vaccination), what will it take to have broad adoption of new prevention and treatment modalities?**

# *Radiosensitivity and Infection-Related Cancers*



- Clues to discovery of infections that cause tumors
- Reduced radiation doses, patient-sparing effective treatment for tumors caused by infections

# *Median Radio Sensitivity Index (RSI) by Tumor Type*

<b>Likely Viral-Related Sites</b>	<b>N</b>	<b>Median RSI</b>
Cervical SCCa	32	0.31
Oropharyngeal SCCa	10	0.32

<b>Mixed Viral-Related Sites</b>	<b>N</b>	<b>Median RSI</b>
Hepatocellular Carcinoma	48	0.25
Vulvar SCCa	4	0.38
Non-Oropharyngeal H&N SCCa	95	0.39

<b>Non Viral-Related Sites</b>	<b>N</b>	<b>Median RSI</b>
Brain Glioma	174	0.58
Melanoma	115	0.49
Pancreatic Adeno	278	0.44
Rectal Adeno	113	0.46
Sarcoma, Abd, RP, Pelv, Ext	80	0.56

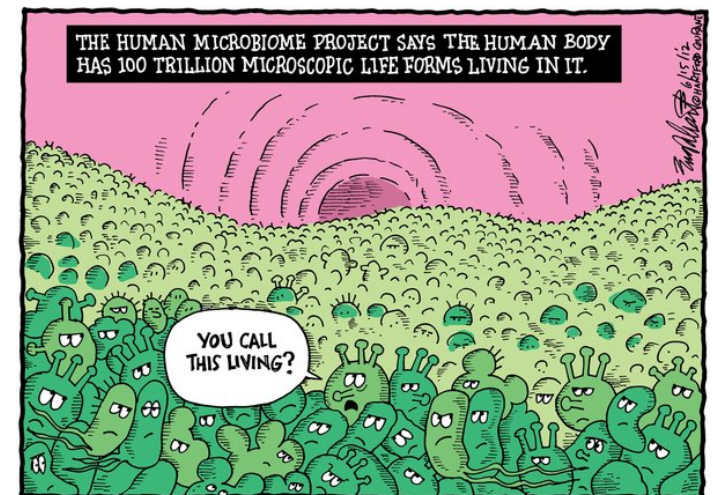
# *Infections: Preventable through Vaccination*



- Extending the benefits of prevention vaccines to other infection and cancer endpoints (head and neck cancers)
- Extending the benefits of immunotherapeutic approaches to cancers caused by infection (anti-PD1, TIL therapy)

# Build Capacity in New Area of Research: The Microbiome

- Completed a search for a Cancer Epidemiology/CIRC assistant faculty member
  - *Christine Pierce Campbell, PhD* appointed July 2014
- Funded Pilot Projects:
  - Tumor microbiome profiles and clinical response to head and neck cancer treatment
  - Metagenomic characterization of the tracheobronchial and lung microbiome of lung cancer patients



**Thank you!**