• My uncle (died age 41, colon cancer)
• My aunt (breast cancer, age 44)
• My grandmother (breast cancer, age 80)
• My uncle (prostate cancer, age 57)
• My great aunt (breast cancer, age 74)
  • My cousin (breast cancer, age 46)
  • My cousin (prostate cancer, age 50)
  • My close friend (multiple myeloma, age 63)
  • Another friend (died age 40, breast cancer)

My Why...Alive Today Because of Clinical Research

My why...the science...the survivors, their strength and their stories
2019 Scientific Retreat
Friday, April 26, 2019
Discovery World Pavilion

Together, Taking on Cancer’s Toughest Challenges
2019 Scientific Retreat
Friday, April 26, 2019
Discovery World Pavilion

Together, Taking on Cancer’s Toughest Challenges
mcw.edu/departments/cancer-center

CENTER UPDATE
Interim Co-Directors
Hallgeir Rui, MD, PhD &
James P. Thomas, MD, PhD

@MCWCancerCenter
Together, Taking on Cancer’s Toughest Challenges...

Why did we chose this as the theme of our retreat?
2019 Scientific Retreat
Together, Taking on Cancer’s Toughest Challenges
TOUGH CHALLENGES IN OUR AREA

• Hyper-segregation “Back in Time 60 Years” – Toronto Star
• Poverty
• Lack of access to healthcare, insurance
• Highest Incarceration Rates in U.S.
• Food deserts
• Obesity
• Tobacco, alcohol and drug use
• Low health literacy
TOUGH CHALLENGES & UNIQUE SOLUTIONS

PANCREAS CANCER

- Risk Factors Unique to WI and Milwaukee: High Rates of Obesity, Type II Diabetes, Alcohol Use
- Milwaukee Metro pancreas cancer incidence rates are significantly higher than in state or nation
- Milwaukee County assigned NCI Priority Index 1 for pancreas cancer in 2014

- Beacon Clinical Program led by Dr. Doug Evans
- Largest clinical pancreas cancer research program in the U.S
- Well funded basic research identifying druggable targets
- Funded social determinants research in breast and prostate survivorship also proving applicable to pancreas cancer prevention
TOUGH CHALLENGES & UNIQUE SOLUTIONS

MULTIPLE MYELOMA

• African Americans in Milwaukee have over triple the incidence rate for multiple myeloma than their white counterparts

• Myeloma treatment has become increasingly complex, expensive and burdensome for patients
  o Rural and poor patients need access to sub-specialists and supportive services

• Beacon Clinical Program led by Dr. P. Hari

• Multiple IITs leading to practice changing results ranging from prevention to late-stage disease

• New recruits in basic MM research are identifying druggable targets and developing new immunotherapeutic approaches
TOUGH CHALLENGES & UNIQUE SOLUTIONS

PROSTATE CANCER

- Significant disparities exist in Milwaukee’s African American communities
- Black men in the Milwaukee Metro area are *twice as likely* to die from prostate cancer as white men
- A need for African American physicians, urologists and oncologists to build trust, increase screening rates, and improve follow up

2019 Scientific Retreat——Together, Taking on Cancer’s Toughest Challenges

UNIQUE SOLUTIONS

- Prostate Cancer Center of Excellence
  - Collaboration from cells to society
  - Recruiting
  - Pilot Funding
- NCI funded community-engaged research on prostate cancer survivorship in African American men
- MCWCC pipeline programs to develop minority prostate cancer researchers, physician scientists and clinical research professionals
TOUGH CHALLENGES & UNIQUE SOLUTIONS

BREAST CANCER

• Significant disparities in Milwaukee’s African American (AA) communities

• Wisconsin tied for worst AA/Caucasian breast cancer mortality rate ratio

• NCI funded research from lab to community and back

• Multidisciplinary working group leading to collaborations and multi-PI RO1s

• Strength in outcomes research is changing policies and practices nationwide

• NCI funded community-engaged research on survivorship for metastatic and Latina breast cancer patients

AA/Caucasian breast cancer mortality rate ratio by state
TOUGH CHALLENGES & UNIQUE SOLUTIONS

PEDIATRIC CANCER

• 200 new cancer patients; 1200 patients receiving treatment in any given year
• Need for tailored and targeted treatments
• Late effect problems

UNIQUE SOLUTIONS

Immunotherapy
• CAR-T cells:
  • Medin: IL12 modified cells for AML
  • Schloemer: developing for osteosarcoma
• NK cells:
  • Pediatric STIR Trials - leukemia and solid tumors

Epigenetic modification therapy
• Burke: Leukemia, now opening nationally in TACL
TOUGH CHALLENGES & UNIQUE SOLUTIONS

BMT

24,000 Hematopoietic Stem Cell Transplants (HCTs) annually in US, BUT

• Only ~1/2 of people who need one, get one:

Access

• Only ~1/2 of people who get one become long-term survivors:

Mortality

• ~1/2 of long-term survivors have significant morbidities:

Quality of Life

• Probability of optimal HLA-matched donor lower in minority populations (75% for whites vs 17-37% for minorities)

International leadership in transplantation research, data collection and prospective clinical trials.

Use of real world data to study HCT and emerging cellular therapies in:

• Strategies to decrease morbidity and mortality

• Long-term follow-up after CAR-T cells

• Coverage with evidence development studies

Trials exploring use of HLA-mismatched related and unrelated donors to serve HLA-diverse populations

Trials exploring use of HLA-mismatched related and unrelated donors to serve HLA-diverse populations
Together, Taking on Cancer’s Toughest Challenges…

EXCITING DEVELOPMENTS, ACCOMPLISHMENTS AND GROWTH in FY2019
CANCER PUBLICATION GROWTH

Cancer Publications by MCW Authors

- 1998: 94
- 1999: 104
- 2000: 113
- 2001: 113
- 2002: 133
- 2003: 145
- 2004: 153
- 2005: 147
- 2006: 171
- 2007: 146
- 2008: 197
- 2009: 182
- 2010: 225
- 2011: 253
- 2012: 277
- 2013: 295
- 2014: 326
- 2015: 350
- 2016: 407
- 2017: 417
- 2018: 455
- 2019: 508 (Projected)
NCI FUNDING GROWTH


$4,100,000 $3,500,000 $3,900,000 $3,300,000 $4,400,000 $4,700,000 $5,100,000 $6,500,000 $8,800,000 $11,600,000

Required

$10 M

2019 Scientific Retreat Together, Taking on Cancer’s Toughest Challenges
ANNUAL INTERVENTIONAL ACCRUAL

Calendar Year

Adult and Pediatric Accrual

Tumor Registry – New Pts
FMLH = 4036
CHW = 132
CONGRATULATIONS

We are now a National Cancer Institute National Clinical Trial Network (NCTN) Lead Academic Participating Site (LAPS)

• The MCW Cancer Center joins an elite group of 30 cancer centers in the U.S. as a leader in the National Cancer Institute’s Clinical Trial Network.
• All other centers with this distinction are NCI designated.
• Congratulations and thank you to all of the faculty, staff, patients and partners who made this possible.
Daily pre-treatment MR imaging with improved soft tissue contrast and motion management reduces planning target volume, more precise TX delivery and opportunity for daily plan adaption

- MCW leading a worldwide consortium on the use of MRI-linac in cancer
- One of only 2 in the U.S. and 7 in the world
SPARCC
Student-Centered Pipeline to Advance Research in Cancer Careers

The goal of SPARCC is to improve and advance diversity and culturally responsive care in the field of clinical cancer research.

The Program Includes:
• Face-to-face workshops at the Medical College of Wisconsin
• Practicum rotations in various cancer-related specialties
• Work and learn alongside recognized researchers and physicians
• Professional development opportunities to seek advanced graduate degrees and employment
• A stipend to support research and learning efforts

PI: Janet Rader, MD
Jack A. & Elaine D. Klieger Professor and Chair of the Department of Obstetrics and Gynecology
March 2019: Governor Evers and Lieutenant Governor Barnes visited MCW to announce $15 million in the state budget to kickstart a new $100M cancer research building on campus.

This building will facilitate heightened collaboration between researchers and physician scientists and bring the newest treatments, approaches and biotech through the translational research pipeline and to Wisconsin patients and communities.
KEEP CRUSHING IT!

In year one:

• Over **1,500** people registered & participated!
• Over **250,000** total mileage goals!
• Thousands of social media posts and shares
• Over **$300,000** raised

2019 CANCER CRUSH is Saturday, September 28
WHAT TO EXPECT IN FY2020?

• Programs, events, and other multidisciplinary activities to build even more collaboration...collaboration... COLLABORATION!

• A focus on supporting and facilitating innovative and impactful cancer research

• Continued investment in community outreach and engagement.

• Enhanced mentorship and pilot programs, through mid-career.

• Team and relationship building, including the continuation of the...
If you want to go fast, go alone.

If you want to go far, go together.

– African Proverb

SEE YOU THIS AFTERNOON for the CANCER COLLABORATIVE
Douglas R. Lowy, MD

- Acting Director, NCI
- NIH Distinguished Investigator
- Chief of the Laboratory of Cellular Oncology, NCI/CCR

Control of HPV-Associated Cancer by Vaccination and Screening
Control of HPV-associated Cancer by Vaccination and Screening

Douglas R. Lowy
Laboratory of Cellular Oncology, Center for Cancer Research
National Cancer Institute, National Institutes of Health

Medical College of Wisconsin Cancer Center
April 26, 2019

The views expressed are my own and do not necessarily reflect those of NCI/NIH
Disclosures

• National Institutes of Health (NIH) has patents on papillomavirus L1 virus-like particle (VLP) vaccine technology. I am an inventor.

• NIH has licensed L1 VLP technology to Merck and GlaxoSmithKline, the two companies with commercial versions of the vaccine.

• I will discuss potential off-label uses of the FDA-approved vaccines: protecting against HPV-positive oropharynx cancer and fewer vaccine doses

• Licensees of other NIH technologies of which I am an inventor: GlaxoSmithKline, Sanofi, Shanta Biotech, Cytos Biotech, Aura Biosciences, Etna Biotech, Acambis, PanVax
Today’s topics

• Cancers induced by HPV and other infectious agents
• HPV vaccines: composition, safety, immunogenicity, efficacy, mechanisms of action, utilization
• Cervical cancer screening: To reduce cervical cancer incidence and mortality while waiting for impact from HPV vaccination; another area of intense investigation
Cancers induced by HPV and other infectious agents
Infectious Agents cause 15-18% of Cancer Worldwide: Rates are higher in LMIC’s than in HIC’s


Adapted from Plummer et al, Lancet Glob Health 4: 609-16, 2016
Epidemiology of HPV-associated Cancers: It depends on where you live
Cervical cancer mortality rates will continue to increase in less developed regions of the world

Less developed regions: Where ~90% of worldwide cervical cancer deaths occur; where cervical cancer accounts for ~10% of female cancer deaths; where cervical cancer represents ~90% of HPV-associated cancer

Projections developed from Globocan 2012
Cervical cancer: A largely preventable cancer with wide global disparities

From Bray et al, Global cancer statistics 2018, Cancer 2018
USA: HPV-associated cancers affect both sexes

- Total number of HPV-positive cancers = ~33,000. 60% women; 40% men
- HPV16/18: Accounts for ~70% of cervical cancers, ~90% of non-cervical cancers
- Pap screening has reduced cervical cancer incidence by ~80%
- Incidence of HPV-positive oropharynx cancer 1988-2004 increased >3-fold

Adapted from Van Dyne, et al., MMWR, 2018; https://www.cdc.gov/cancer/hpv/statistics/cases.htm
Cervical cancer natural history and prevention

Natural history is universal: Same in high- and low-resource settings

Wentzensen and Schiffman Lancet Public Health 2017
HPV Vaccines
Collaborators

Laboratory of Cellular Oncology, CCR, NCI

John Schiller

Patricia Day                  Nicolas Cuburu
Rhonda Kines                Susana Pang
Cynthia Thompson            Alessandra Handisurya
Lukas Bialkowski            Alex Bell

Chris Buck, Diana Pastrana - LCO, CCR, NCI Bethesda
Aimee Kreimer, Allan Hildesheim, Mark Schiffman, Mahboobeh Safaeian, Ligia Pinto - DCEG, NCI, Bethesda
Peter Choyke, Marcelino Bernardo - Molecular Imaging, CCR, NCI, Bethesda
Jeffrey Roberts – FDA, Rockville
Rolando Herrero – IARC, Lyon, France
Bryce Chackerian - University of New Mexico
Reinhard Kirnbauer - University of Vienna, Austria
Key issues for HPV vaccine development

- No precedent for a successful vaccine against a local sexually transmitted infection
- Protective immunity thought to be attributable to neutralizing antibodies
- Not clear how to make a vaccine that would induce high levels of neutralizing antibodies

Solution: A subunit vaccine of virus-like particles (VLPs); composed of the main protein that makes the outer shell of the virus (L1); L1 contains the immunodominant neutralization epitopes
Prophylactic HPV Vaccines Are L1 Virus-Like Particles (VLPs)

L1 Insertion into a Baculovirus Expression Vector

Production in Insect Cells

Spontaneous assembly of 360 copies of L1 into a VLP

Induce high titers of virion neutralizing antibodies

Non-infectious, Non-oncogenic

Reinhard Kirnbauer et al. PNAS 1992
Quadrivalent HPV vaccine safety review and safety monitoring plans for nine-valent HPV vaccine in the United States

Julianne Gee, Cindy Weinbaum, Lakshmi Sukumaran, and Lauri E. Markowitz

Division of Healthcare and Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA; Division of Viral Diseases, National Center Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA

ABSTRACT
Quadrivalent human papillomavirus (4vHPV) vaccine was licensed for use in the United States in 2006 and through 2015 was the predominate HPV vaccine used. With the exception of syncope, a known preventable adverse event after any injected vaccination, both pre-licensure and post-licensure 4vHPV safety data have been reassuring with no confirmed safety signals identified. Nine-valent HPV vaccine (9vHPV) was licensed in 2014. This review includes post-licensure 4vHPV safety findings published to date that have informed the US vaccination program; these data will inform US safety monitoring and evaluation for 9vHPV.

See also Philips et al, Safety of Human Papillomavirus vaccines: an updated review. Drug Safety 41:329-46, 2018
High efficacy of HPV L1 VLP vaccines against new cervical precancer and genital warts by vaccine-targeted types in randomized trials

In women with no genital HPV infection detected in at the start of each trial

<table>
<thead>
<tr>
<th>End Point</th>
<th>Sex</th>
<th>Age</th>
<th>Vaccine</th>
<th>Targeted HPV Types</th>
<th>Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precancer</td>
<td>Female</td>
<td>15-26</td>
<td>Quadrivalent / Gardasil</td>
<td>HPV 6, 11, 16, 18</td>
<td>100% (85.5-100)</td>
</tr>
<tr>
<td>Genital Warts</td>
<td>Female</td>
<td>15-26</td>
<td>Quadrivalent / Gardasil</td>
<td>HPV 6, 11, 16, 18</td>
<td>96.4% (91.4-98.4)</td>
</tr>
<tr>
<td>Precancer</td>
<td>Female</td>
<td>15-25</td>
<td>Bivalent / Cervarix</td>
<td>HPV 16, 18</td>
<td>100% (90.5-100)</td>
</tr>
<tr>
<td>Precancer</td>
<td>Female</td>
<td>16-26</td>
<td>Nonavalent / Gardasil-9</td>
<td>HPV 6, 11, 16, 18, 31, 33, 45, 52, 58</td>
<td>97.1% (83.5-99.9)</td>
</tr>
</tbody>
</table>

Precancer = Cervical Intraepithelial Neoplasia Grade 3
Lehtinen Lancet Oncol 2011; Munoz JNCI 2010; Huh Lancet 2017
First successful vaccines against a local sexually transmitted infection  
2016: 9-valent vaccine approved for 2 doses for 9-14 year olds
HPV vaccination (quadrivalent) rapidly reduced development of new cervical precancers in young women in Australia

Goals of HPV Vaccination

• Directly reduce risk of infection and disease in vaccinees

• Indirectly reduce risk by reducing prevalence of “HPV vaccine types” in general population (herd immunity)
Herd Immunity: Decreased incidence of genital warts in heterosexual Australian men following female HPV vaccine implementation in 2007

Genital wart trends in men in the United States: Relationship to age and HPV vaccination

Flagg & Torrone, Am J Public Health 108:112-119, 2018
Genital wart trends in women in the United States: Relationship to age and HPV vaccination

Flagg & Torrone, Am J Public Health 108:112-119, 2018
Scotland: Herd immunity & HPV type cross-protection in women from bivalent vaccine

Cavanagh et al, Lancet Infect Dis 17:1293-1302, 2017

Similar results for the quadrivalent vaccine in Australia against HPV16/18: Chow et al, Lancet Infect Dis 17:68-77, 2017
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Similar results for the quadrivalent vaccine in Australia against HPV16/18: Chow et al, Lancet Infect Dis 17:68-77, 2017
In Black and Hispanic women, 9-valent HPV vaccine may be especially useful for preventing more precancers

From Saraiya et al, JNCI, 2015

<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>Black</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cervical cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV16/18</td>
<td>67%</td>
<td>68%</td>
<td>64%</td>
</tr>
<tr>
<td>HPV31/33/45/52/58</td>
<td>12%</td>
<td>15%</td>
<td>18%</td>
</tr>
<tr>
<td>Total</td>
<td>79%</td>
<td>83%</td>
<td>82%</td>
</tr>
<tr>
<td><strong>In situ cervical cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>HPV16/18</td>
<td>67%</td>
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<td>16%</td>
<td>37%</td>
<td>26%</td>
</tr>
<tr>
<td>Total</td>
<td>83%</td>
<td>64%</td>
<td>76%</td>
</tr>
</tbody>
</table>
Trends in U.S. Vaccination Rates: Ages 13-17 Years

FIGURE. Estimated coverage with selected vaccines and doses* among adolescents aged 13–17 years, by survey year and ACIP recommendations† — National Immunization Survey-Teen, United States, 2006–2017§
## 2017 HPV and Meningococcal Vaccination Rates for 13-17 year olds

<table>
<thead>
<tr>
<th></th>
<th>HPV vaccine (≥1 dose)</th>
<th>Meningococcal vaccine (≥1 dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>65%</td>
<td>85%</td>
</tr>
<tr>
<td>Below poverty</td>
<td>73%</td>
<td>86%</td>
</tr>
<tr>
<td>At or above poverty</td>
<td>63%</td>
<td>85%</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>69%</td>
<td>84%</td>
</tr>
<tr>
<td>Indiana</td>
<td>59%</td>
<td>93%</td>
</tr>
<tr>
<td>Kansas</td>
<td>52%</td>
<td>72%</td>
</tr>
</tbody>
</table>

From MMWR August 24, 2018
Higher HPV vaccine uptake in states with lower incidence of HPV-associated cancer
Polio vaccine: 1950’s
Polio vaccine: 1950’s
HPV vaccination is the best way to PREVENT many types of CANCER.

HPV vaccination is RECOMMENDED at ages 11 or 12.

HPV vaccination is REDUCING HPV DISEASE.

3 THINGS PARENTS SHOULD KNOW ABOUT PREVENTING CANCER

www.cdc.gov/vaccines/teens
One more complication: A worldwide HPV vaccine shortage


• Secondary to increased vaccine demand

• The shortage is projected to last several years

• Question: During this period, should there be policy implications in the industrialized world when considering adding gender-neutral vaccination or increasing the age range for recommending vaccination?
High Efficacy of VLP Vaccine

- Repetitive structure of VLP intrinsically immunogenic
- Tissue-associated neutralizing antibodies exudated at potential sites of infection
  - Levels of exudated antibodies high, similar to serum levels, not lower levels of non-disrupted genital tract
- HPV highly susceptible to neutralizing antibodies
- For further discussion: see Schiller & Lowy, Vaccine 2018
Neutralizing L1 Antibodies (in red) Bound to Papillomavirus Particle
High titer antibodies induced by HPV vaccination prevent basement membrane binding

Based on Patricia Day et al, Cell Host Microbe 16: 260-70, 2010
The challenge to global HPV vaccination

• 107 million girls 10-14 years old have received at least one dose of the HPV vaccine
The challenge to global HPV vaccination

- 107 million girls 10-14 years old have received at least one dose of the HPV vaccine
- However, <5% of eligible girls have been vaccinated in Low-and Middle-Income Countries (LMICs), where ~90% of cervical cancer deaths occur
- Worldwide >60 million girls are now born annually
- To control of cervical cancer worldwide, should vaccinate 40-50 million girls in each birth cohort
Might a single HPV vaccine dose confer years of protection?
Post-hoc evidence for protection from a single vaccine dose

- **Bivalent vaccine:** Costa Rica vaccine trial; Safaien et al, JNCI 2017; Kreimer et al, Vaccine 2018
- **Quadrivalent vaccine:** IARC India trial; Sankaranarayanan et al, Lancet Oncol 2016; Sankaranarayanan et al, Vaccine 2018
- Insufficient evidence to change standard of care, but sufficient evidence to warrant rigorous evaluation of single dose potential
The Costa Rica Vaccine Trial: Prevalent HPV infection 11 years after bivalent HPV vaccination: One dose is not inferior to three doses (post-hoc analysis)
Stable HPV16 serum antibodies 11 years after one dose of the bivalent HPV vaccine (post-hoc analysis)

100% of 1 dose recipients remain seropositive at 11 years

HPV 16 Antibody Geometric Means (EU/mL)

- 3 doses
- 2 doses (0/6)
- 1 dose

Natural Immunity
Dense Repetitive Epitope Array Is the Key To Potent Antibody Induction by HPV VLPs

BCR/Monomeric Protein Complexes

Weak Activation Signals
Low Level Antibodies
Short duration

Strong Survival/Proliferation Signals
High Level Antibodies
Long Duration

Tyrosine Kinase

Oligomerization of BCR by Ag Induces Long-Live Plasma Cells.
Randomized controlled trial in Costa Rica to test efficacy of 1 dose vs. 2 doses (NCI & Gates Foundation)

- 4-arm: 1 vs. 2 dose Cervarix
  1 vs. 2 dose Gardasil9
- 5000 12-16 year old females per arm
- Survey of HPV prevalence in region
- 4 year primary trial, longer term follow-up
- For more information: see clinicaltrials.gov; Identifier NCT03180034; Aimee Kreimer et al, Vaccine 2018
Potential impact of demonstrating 1 dose can confer strong protection

• Could change standard of care in US & globally
  – Could save US > $300 million each year in vaccine costs

• Could make it feasible to control the worldwide public health problem of cervical cancer and other HPV-associated cancers
Use repetitive structure to increase vaccine immunogenicity

- **Candidate VLP vaccines against BKV & JCV**

- **Candidate ferritin-based vaccines against influenza and EBV**
Cervical cancer screening: It’s now etiology-based
Cervical cancer in the USA: Incidence in black women is now similar to white women; mortality disparity remains

Cervical cancer Incidence: SEER data

Current mortality rates
ASR* 2012-2016

Black women: 3.5
White women: 2.2

*ASR=Annual Standardized Rate
HPV-based testing for primary cervical cancer screening

- In vaccinated populations, HPV-based testing for cervical cancer screening will identify more HPV infections with precancer than will cytology.

- USPSTF recommendations:
  - HPV-based testing every 5 years for primary cervical cancer screening for women 30-65.
  - Cytology testing every 3 years, for women 21-65.
Cervical Cancer Screening: From Pattern Recognition to Molecular Diagnosis

• **Cytology-based screening: pattern recognition**

• Has reduced cervical cancer incidence and mortality (~80% in the USA)
  – However, expensive, requires specialized expertise in cytology

• **HPV screening: etiology-based.** More sensitive, better at detecting adeno precancer, higher positive and negative predictive value, more readily exportable to low resource settings
However, many HPV infections do not need to be treated

• Many HPV-positive women do not need to be treated because they do not have precancer
  – Many HPV infections go away without treatment before the lesions become precancerous

• Ancillary testing: For triage of HPV-positive women; various triage tests under study
Clinical performance of viral methylation

- Now developing **integrated HPV detection, genotyping, and methylation assay**
- Evaluation in self-collected specimens

Clarke 2018 Clin Cancer Res
Cervical cancer screening by visualization with acetic acid (VIA): Artificial intelligence may convert VIA from an inferior test to a viable one

• Visualization of the cervix with acetic acid is an inferior screening test
• However, machine learning & artificial intelligence from digitized images – automated cervical evaluation (AVE) - can greatly increase the ability of this approach to detect cervical precancer

Data developed from Guanacaste natural history study
A 42 year old woman with LSIL cytology and HPV16 has a n% risk of CIN3+, which is above the colposcopy referral threshold of m%.
Henrietta Lacks (HeLa cells) had Cervical Adenocarcinoma

- Pap smear screening: more sensitive for squamous cell carcinoma than adenocarcinoma
- ~90% of cervical adenocarcinoma caused by HPV16 or HPV18
- Henrietta Lacks: HPV 18 cervical adenocarcinoma not detected by cytology
- Her cancer should now be preventable by HPV vaccination or by HPV-based screening
Summary and Conclusions

- Basic research led to identification of HPV as the cause of several cancers and to development of the HPV vaccines and HPV-based cervical cancer screening

- Virus-like particle display is highly immunogenic; the induced antibodies are durable
  - Probably attributable to long-lived plasma cells induced by repetitive display in the vaccine

- Control of HPV-associated cancer as a worldwide public health problem may soon be feasible