COVID-19 and Cancer Research

Paula J. Bates, PhD
Longtime Cancer Researcher
Recent COVID-19 Researcher
Passionate About Innovation
Brown Cancer Center, University of Louisville

Disclosures for P. Bates: patents pending; research funding from UPS and Qualigen, Inc.

About Me …

Researcher

cancer, drug discovery, **translation**

Inventor

14 issued US patents

Entrepreneur

Aptamera co-founder

Collaborator

Antisoma, Transmed, Qualigen

Mentor

students and faculty entrepreneurs

Program Director

ExCITE – UofL product development

KYNETIC – statewide innovation

My Journey

Nantwich
high school (1988)

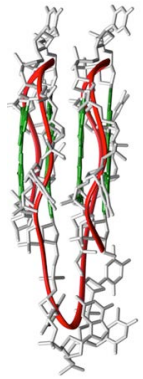
Oxford
BA, Chemistry (1992)

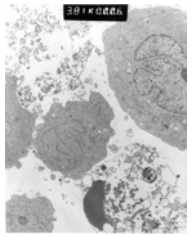
London
PhD, Biophysics (1996)

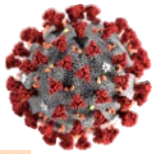
Birmingham, AL
postdoc, Molecular Biology (1999)

Louisville, KY
faculty (since 1999)

My Research

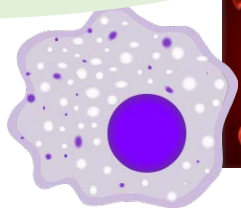


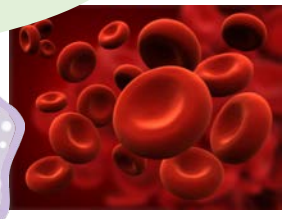




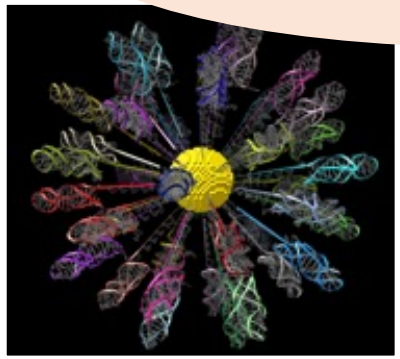
Aptamer
cancer and COVID-19

Collaborative
cancer immunotherapy, blood

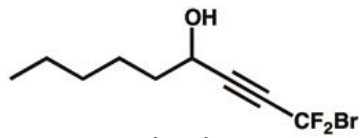


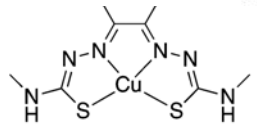


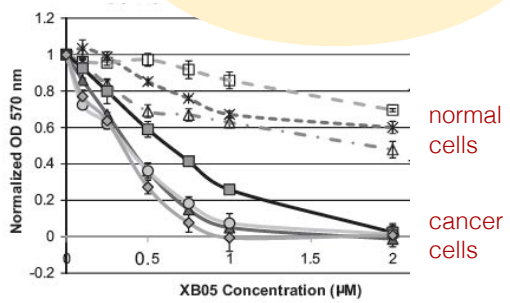
Nanotechnology
cancer



Therapies
cancer







Innovation
product development

EXCITE
an NIH REACH Hub
Expediting Commercialization, Innovation, Translation & Entrepreneurship

KYNETIC
Kentucky Network for Innovation and Commercialization

Why are cancer researchers studying COVID-19?

to overcome the virus

- COVID-19 is making cancer care more challenging.

to protect cancer patients

- Cancer patients are at increased risk of COVID-19.

to answer questions about cancer and COVID-19

- Do cancer therapies affect COVID-19 outcomes?
- Understand immune responses to cancer & virus.

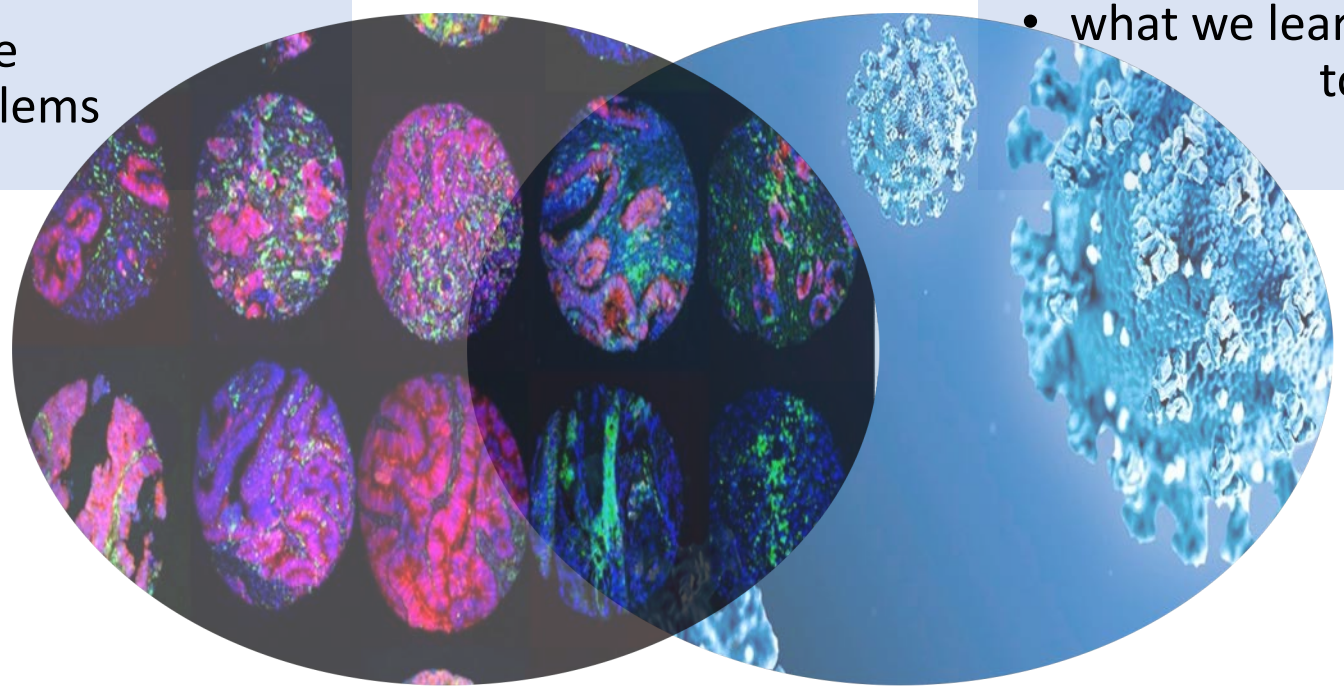
Overlaps between cancer and COVID-19?

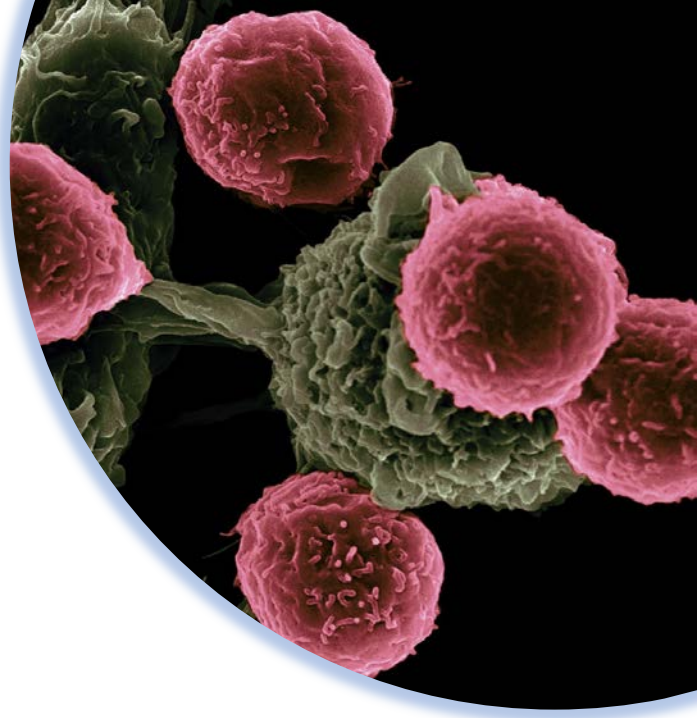
Our immune system

- can detect virus/abnormal cells
- protects us against COVID/cancer
- active evasion by virus/cancer cells
- inappropriate immune response causes problems

Therapeutics

- some cell surface molecules play a role in both cancer and virus
- repurposed cancer drugs -> COVID
- what we learn from COVID may lead to new cancer therapies





UofL's Brown Cancer Center

- state-of-the-art multidisciplinary cancer care
- national leader in cancer immunotherapy clinical trials
- <u>new</u> $11.5 M grant for cancer immunology research

harnessing the power of the immune system to eradicate cancer

UofL's "Lab-to-Life" Innovation Programs

a national leader in translational research and entrepreneurial education

Program Goals:

- Accelerate the successful translation of ideas into products
- Improve health, education, and the economy in Kentucky
- Encourage multidisciplinary, product-focused research
- Increase the involvement of underrepresented groups in innovation
- Identify and share best practices for research commercialization

Unique Features:

- A focus on changing mindsets (of researchers and institutions)
- We provide funding + training/coaching/mentoring + a network
- Access to and review by industry and federal experts
- Upfront business case review and industry-style project management
- "Fail fast" philosophy – milestones; go/no go; tranched funding

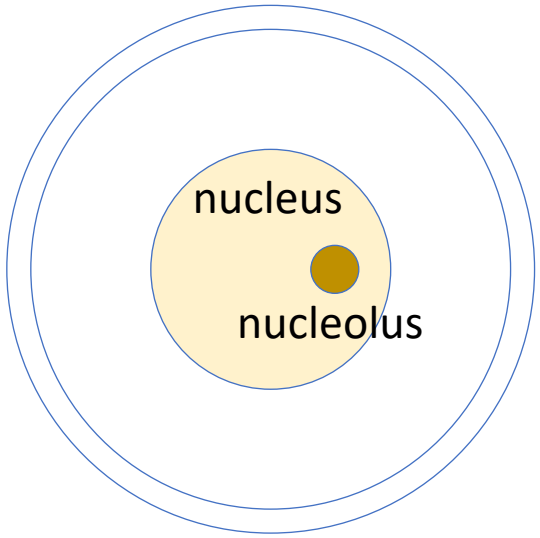
How did I become a COVID-19 researcher?

- January 2020: Start to worry about “the new coronavirus” …
- February 2020: Hatch an idea to inhibit SARS-CoV-2 based on previous research related to nucleolin

Nucleolin and Cancer

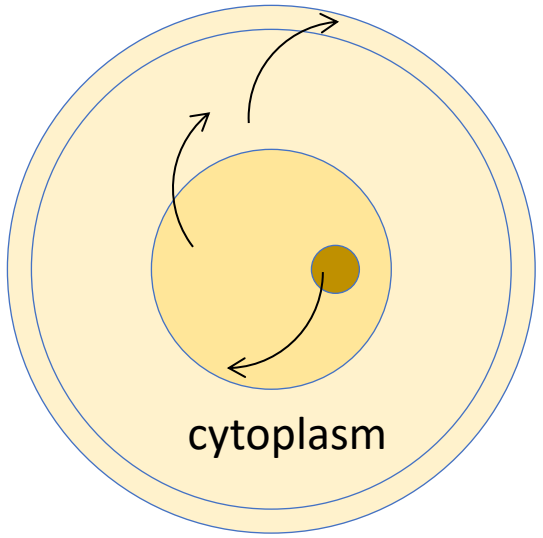
Normal Cell

Nucleolin found only inside the cell



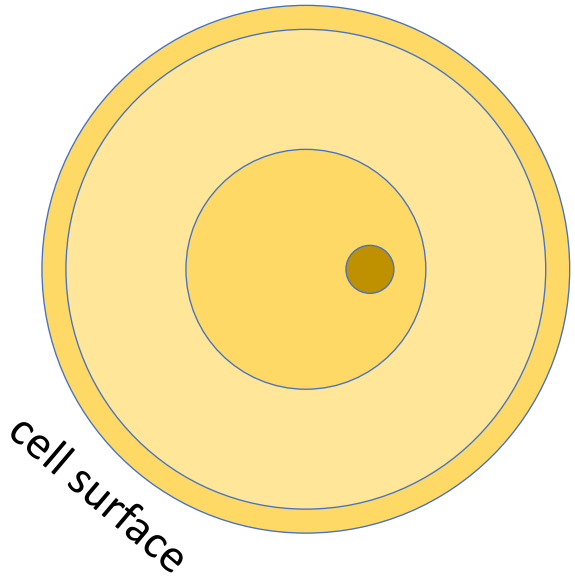
Stressed Cell

Nucleolin moves to cell surface in response to stress or signals



Cancer Cell

Nucleolin present at high levels throughout the cell.



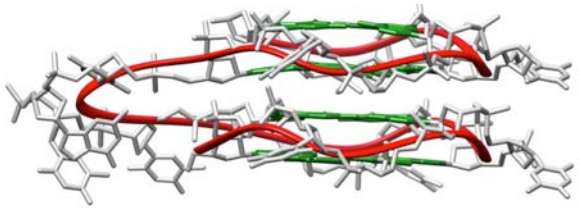
Paula Bates

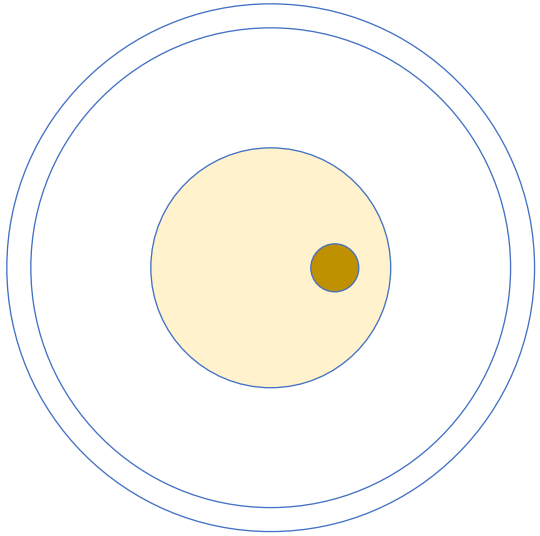
Donald Miller

John Trent

AS1411: A Nucleolin Aptamer

- A short strand of synthetic DNA
- Forms an unusual structure (G-quadruplex)
- Binds specifically to nucleolin protein
- Selectively targets & kills cancer cells

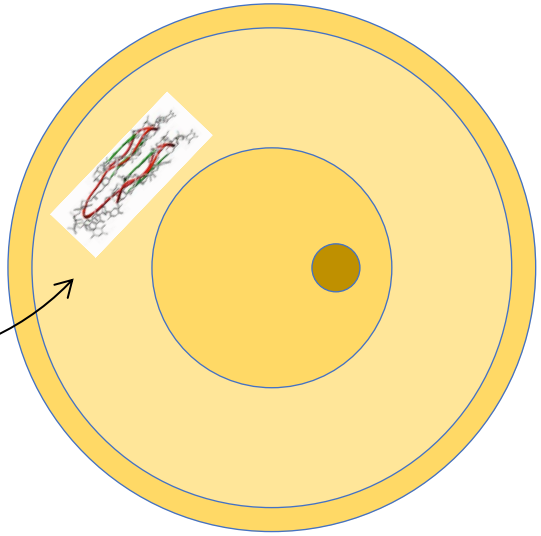




Normal Cell

Nucleolin inside the cell.
Invisible to AS1411.

- Completed Phase 1 & 2 clinical trials
- > 100 cancer patients treated
- No serious side effects due to drug
- Anticancer effects in a few patients



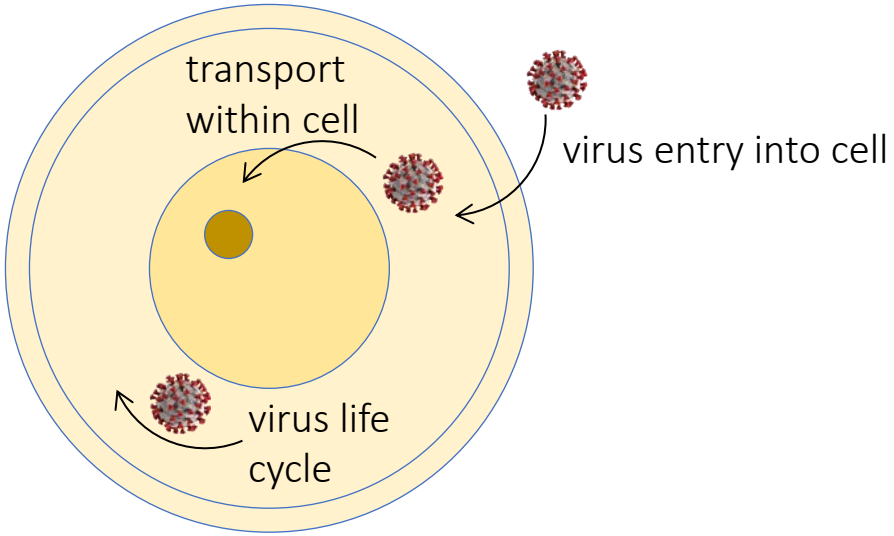
Cancer Cell

Nucleolin present at high levels on the cell surface.

Nucleolin and Viruses

In response to stress or viruses:

Nucleolin moves to the cell surface when cells are infected by some **viruses**. It has been shown to play important roles in virus infectivity:



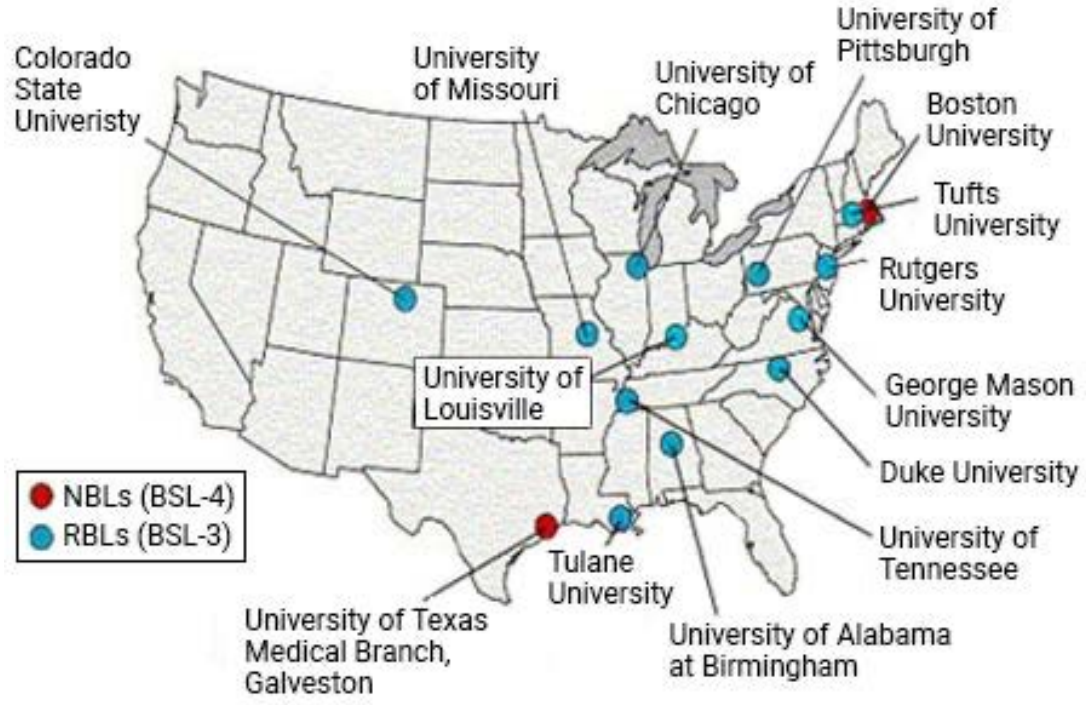
Can the nucleolin aptamer (AS1411) block SARS-CoV-2?

Nucleolin implicated in the biology of …

- HIV-1
- influenza A
- hepatitis C virus
- respiratory syncytial virus (RSV)
- herpes simplex virus 1 (HSV-1)
- human cytomegalovirus (CMV)
- dengue virus
- Epstein-Barr virus (EBV)
- human papilloma viruses (HPV)
- rabies virus
- coxsackie B virus
- enterovirus 71 (EV71)
- parainfluenza virus
- Crimean-Congo hemorrhagic fever virus
- avian IBV coronavirus
- SARS coronavirus (predicted)

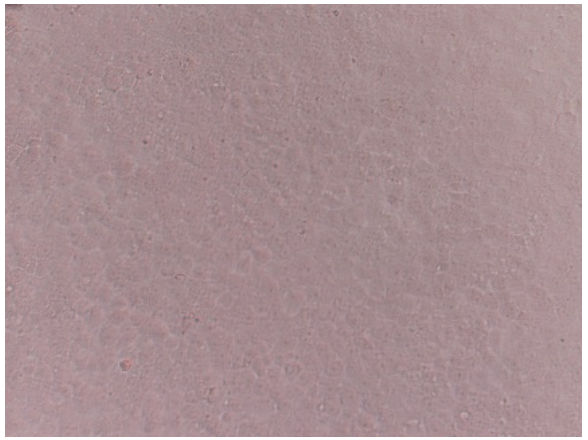
Luckily, I'm in Louisville

February 2020: Discuss idea with Kenneth Palmer, head of UofL's Center for Predictive Medicine and Regional Biocontainment Lab (RBL)

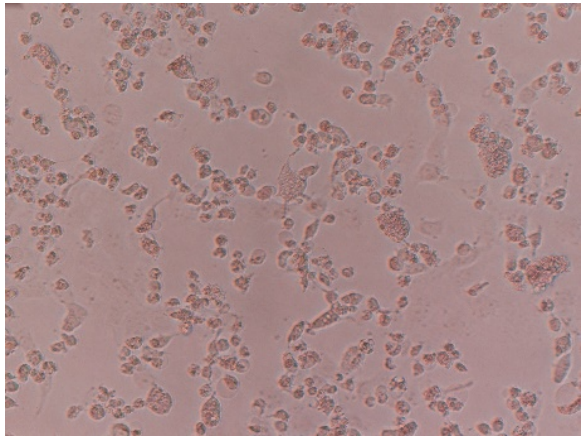


A Eureka Moment …

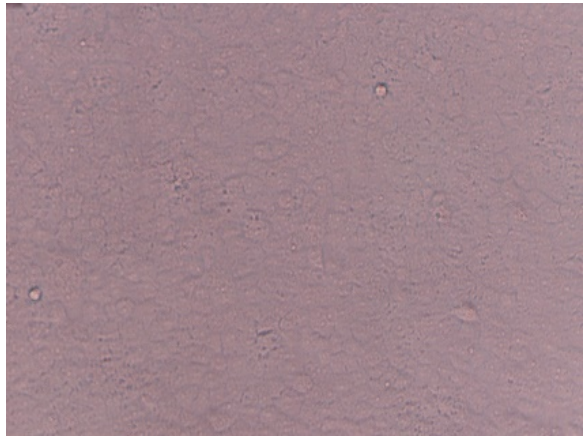
March 2020: First evidence that AS1411 inhibits infection by the COVID coronavirus (SARS-CoV-2)*



Without SARS-CoV-2



Infected with SARS-CoV-2



Infected with SARS-CoV-2
+ treated with AS1411

* Thanks to Kenneth Palmer, Divya Saxena, Jennifer DeMarco, Bill Severson, and all the faculty and staff at the CPM

What's Next for AS1411?

- Experimental drug, expected to be safe based on cancer clinical trials
- Evidence of inhibitory activity against SARS-CoV-2 in multiple assays

- Scale up drug manufacture, additional studies
- FDA authorization for human studies
- Human clinical trials in COVID-19 patients
- Developing new AS1411 formulations for cancer

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