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freenome

Decoding the means to cancer's end

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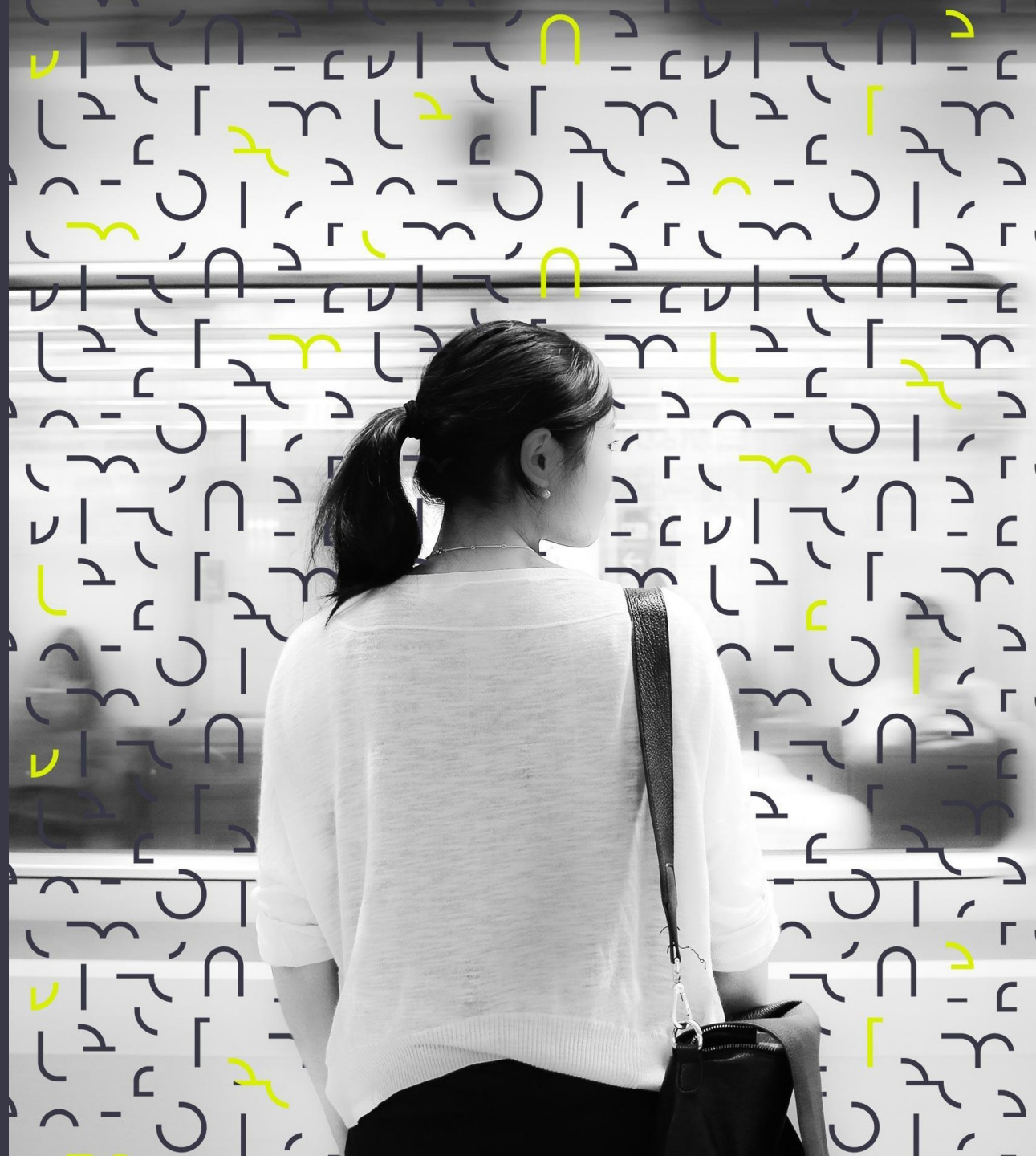
Chief Medical Officer

1July 2020
35th EDRN Steering Committee Meeting



Agenda

- Introduction to Freenome
- “Universal” Cancer Screening: The Opportunity
- Preliminary Comments
- Challenges & Solutions
- Final Thoughts & Questions

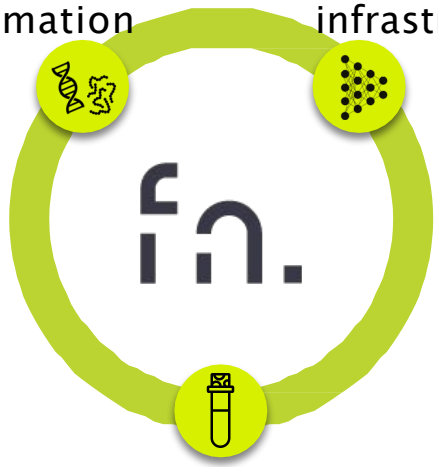
Introduction to Freenome

- Founded in 2014
- Located in South San Francisco
- Multiple academic, clinical, and biopharma collaborators
- 19 publications and presentations to date

Freenome's platform

Cell-free biology, **multiomics platform** enabled by automation

Joint-representation **machine learning** infrastructure and QC



Clinical data feedback loop to improve test and drive outcomes

“Universal” cancer screening: The opportunity

- Screen simultaneously for multiple cancers
- In 2020, cancers for which there is no screening in asymptomatic individuals represent ~52% of new cancer diagnoses and ~56% of cancer-related deaths

Estimated New Cases

Males			Females		
Prostate	191,930	21%	Breast	276,480	30%
Lung & bronchus	116,300	13%	Lung & bronchus	112,520	12%
Colon & rectum	78,300	9%	Colon & rectum	69,650	8%
Urinary bladder	62,100	7%	Uterine corpus	65,620	7%
Melanoma of the skin	60,190	7%	Thyroid	40,170	4%
Kidney & renal pelvis	45,520	5%	Melanoma of the skin	40,160	4%
Non-Hodgkin lymphoma	42,380	5%	Non-Hodgkin lymphoma	34,860	4%
Oral cavity & pharynx	38,380	4%	Kidney & renal pelvis	28,230	3%
Leukemia	35,470	4%	Pancreas	27,200	3%
Pancreas	30,400	3%	Leukemia	25,060	3%
All Sites	**893,660**	**100%**	**All Sites**	**912,930**	**100%**

Estimated Deaths

Males			Females		
Lung & bronchus	72,500	23%	Lung & bronchus	63,220	22%
Prostate	33,330	10%	Breast	42,170	15%
Colon & rectum	28,630	9%	Colon & rectum	24,570	9%
Pancreas	24,640	8%	Pancreas	22,410	8%
Liver & intrahepatic bile duct	20,020	6%	Ovary	13,940	5%
Leukemia	13,420	4%	Uterine corpus	12,590	4%
Esophagus	13,100	4%	Liver & intrahepatic bile duct	10,140	4%
Urinary bladder	13,050	4%	Leukemia	9,680	3%
Non-Hodgkin lymphoma	11,460	4%	Non-Hodgkin lymphoma	8,480	3%
Brain & other nervous system	10,190	3%	Brain & other nervous system	7,830	3%
All Sites	**321,160**	**100%**	**All Sites**	**285,360**	**100%**

Siegel et al., 2020

Preliminary comments

- The question is not the objective; it's how we get there responsibly
- What are the risks, benefits and costs of detecting more cancers for which the clinical utility of detection and intervention have not been demonstrated?
- **Can ≠ should**

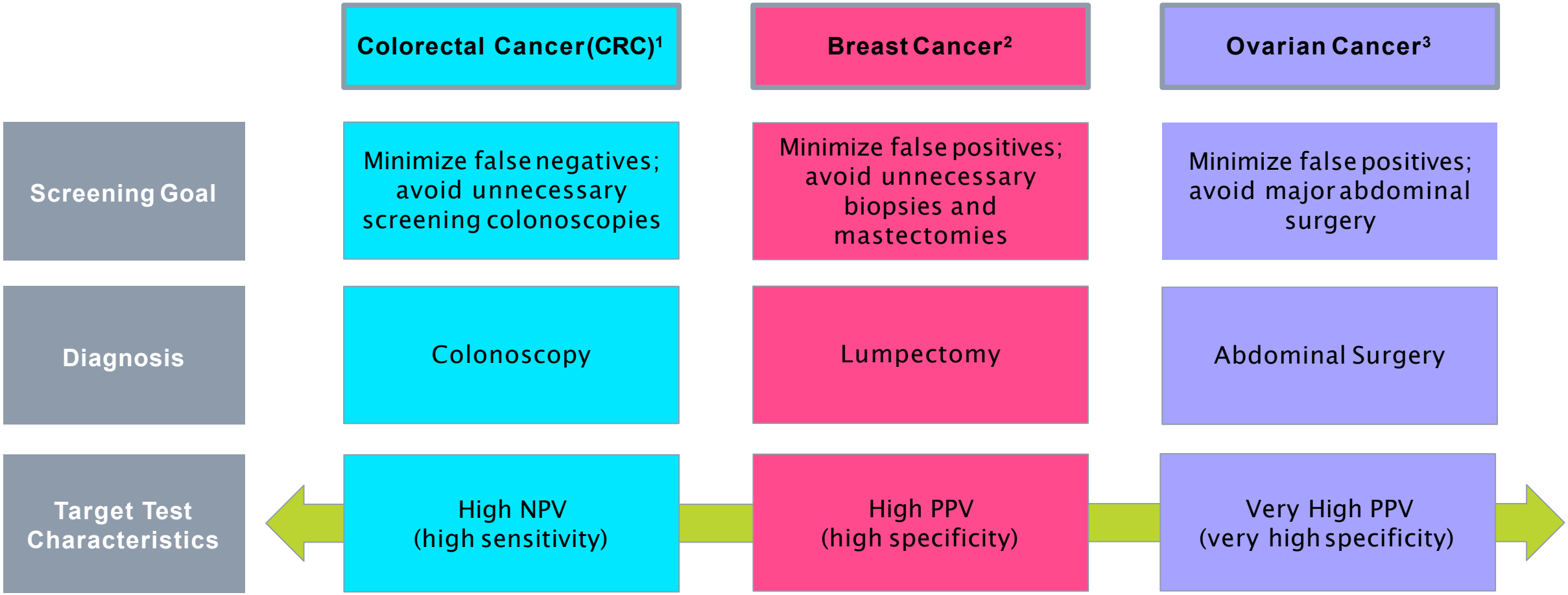
What is “universal” cancer screening?

- There are >100 different types of cancer

- There is currently no test in development or commercially available that is “universal” or “pan”, so to describe as such is inappropriate

- Requirements for such a test
  - Very low false positive rate (<1%) in **unscreened** cancers
  - If include **screened** cancers, comparable or better performance (both **sensitivity** AND **specificity**) versus the existing standard of care taking into consideration **real-world adherence**
  - Very low **tissue-of-origin** misclassification (<1%)
  - Clinical validation in the **intended use population**
  - **Clinical utility** in the intended use population

One size does not fit all in cancer screening



1.Bibbons-Domingo et al., JAMA. 2016; 2. Siu et al., Ann Intern Med. 2016; 3. Grossman et al., JAMA. 2018

One size does not fit all in cancer screening

Cancer Type	Population	Year	Recommendation	
Cervical	Women aged 21to 65 years	2018	A	**Recommended:** Highcertainty that net benefit is substantial.
CRC	Adults aged 50 to 75 years	2016		
Breast	Women aged 50 to 74 years	2016	B	**Recommended:** Highcertainty that net benefit is **moderate** or there is **moderate certainty that the net benefit is moderateto substantial.**
Lung	Adults Aged 55–80, with a history of smoking	2013		

One size does not fit all in cancer screening

Cancer Type	Population	Year	Recommendation Strength	
Prostate	Men aged 55 to 69 years	2018	C	**Recommends selectively offering** or providing this service to individual patients based on professional judgment and patient preferences. There is at least **moderate certainty that the net benefit is small**.
Ovarian	Asymptomatic Women	2018	D	**Recommends against** the service. There is **moderate or high certainty** that the service has **no net benefit** or that the **harms outweigh the benefits.**
Pancreatic	Adults	2019	D	
Thyroid	Adults	2017	D	

One size does not fit all in cancer screening

Cancer Type	Population	Year	Recommendation Strength	
Bladder	Asymptomatic Adults	2011	I	USPSTF concludes that the current **evidence is insufficient** to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the **balance of benefits and harms cannot be determined.**
Skin		2016		

Challenges

- **Low disease prevalence** makes developing a screening test challenging
  - DeeP-C: **12,766** patients enrolled to get **10,023** evaluable samples to get **65** CRCs*
  - As a result, most screening tests are developed using **post-diagnosis samples** (due to cost, time, etc.) and **case-control designs**

- Concerns with such approaches
  - **Generalizability** to asymptomatic patients (i.e., **intended use population**)
  - **Reliability** of "controls" (e.g., negative by history and/or patient self-report)
  - **Spectrum bias** (i.e., absence of full disease spectrum) and lack of potentially **confounding comorbidities**

* SSED, P130017

Spectrum Bias: Cancer Stage & Precancerous Lesions

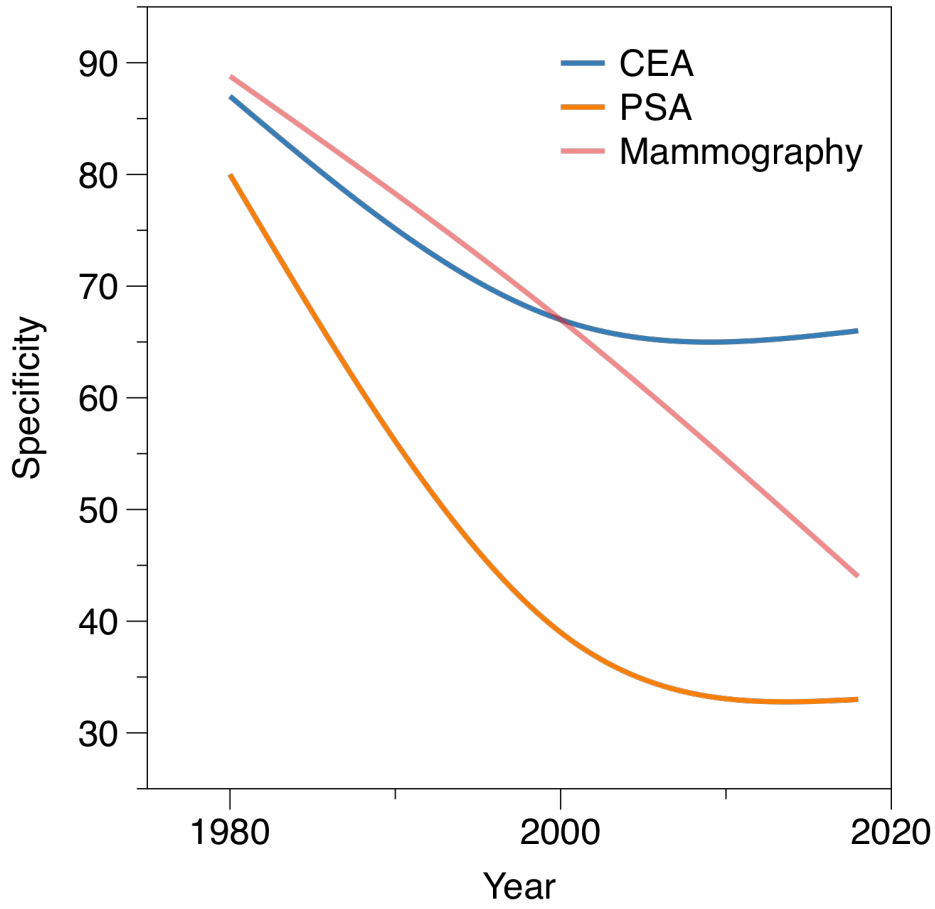
Stage	Imperiale 2014[1] (DeeP-C)	Lidgard 2013[2]	Lennon 2020[3] (DETECT-A)	Cohen 2018[4]
I	45%	22%	51%	20%
II	32%	26%	14%	49%
III	15%	33%	14%	31%
IV	6%	8%	20%	0%
Unknown	2%	11%	1%	NA

Final Diagnosis of Index Lesion	% of Study Population[1]
CRC	1%
Advanced adenoma	8%
Non-advanced adenoma	29%
Negative by colonoscopy and/or histopathology	63%

1.Imperiale et al., *NEJM.* 2014; 2. Lidgard et al., *Clin. Gastroenterol. Hepatol.* 2013; 3. Lennon et al., *Science*. 2020; 4. Cohen et al., *Science.* 2018

Potential solutions

- Shared, **publicly available resources** (e.g., sample banks such as EDRN)
- Using **real-world evidence** (not just traditional clinical trials) for population-scale studies to improve performance over time
- Appropriate balance between **pre- and post-market commitments**
- **Best practice** guidelines



Hofvind S et al. 2012
Shinkins et al. 2017
Komen Foundation 2018
Loughlin K et al. 2011

Final thoughts & questions

- If a multi-cancer test, what is the intended use population?
  - Is there clinical utility for screening in asymptomatic individuals in this population?
- What is the recommended action after a positive test result? After a negative test result (e.g., periodicity of re-screening)?
  - How well do providers and patients follow these recommendations?
  - Is there a net health outcome benefit when they do?
  - What is the impact on the total cost of care when do they do?
- What are the risks from false negative and false positive results?
- Which cancers will be included for screening?
  - If USPSTF A&B cancers are included, what impact does introduction of the test have on standard-of-care screening adherence?
- Was clinical validation performed in the intended use population?
  - Including the full spectrum of disease and comorbid conditions that will be encountered in the intended use population?
  - Using the collection device and process used for routine clinical care?
- Were diagnoses (e.g., cancer, negatives and precancerous lesions) confirmed? How?

freenome


Spot the pattern.
Treat the cancer.

5 minute Q&A

SC Chair/Co-Chair

feed Zoom Q&A to presenter and Track Time

NCI and Production Team

flag Q&A, answer Chat and Slack