TECNOPOLO FERRARA

ASTER
innovazione attiva

Università degli Studi di Ferrara

Finanziamenti europei per ricerca e innovazione:
Le opportunità di Horizon2020 presso i Tecnopoli

FOCUS SALUTE

5 Luglio 2018

presso il Tecnopolo - via Saragat 13 - Ferrara

ROBERTO GAMBARI – Il Progetto ULTRAPLACAD (ULTRAsensitive PLAsmonic devices for early Cancer Diagnosis)

gam@unife.it

Bright ideas and innovative activities

- HORIZON-2020: **ULTRAsensitive PLAsmonic devices for early CAncer Diagnosis**
- *Innovation: ultrasensitive detection, PCR-free, non-invasive diagnostics*

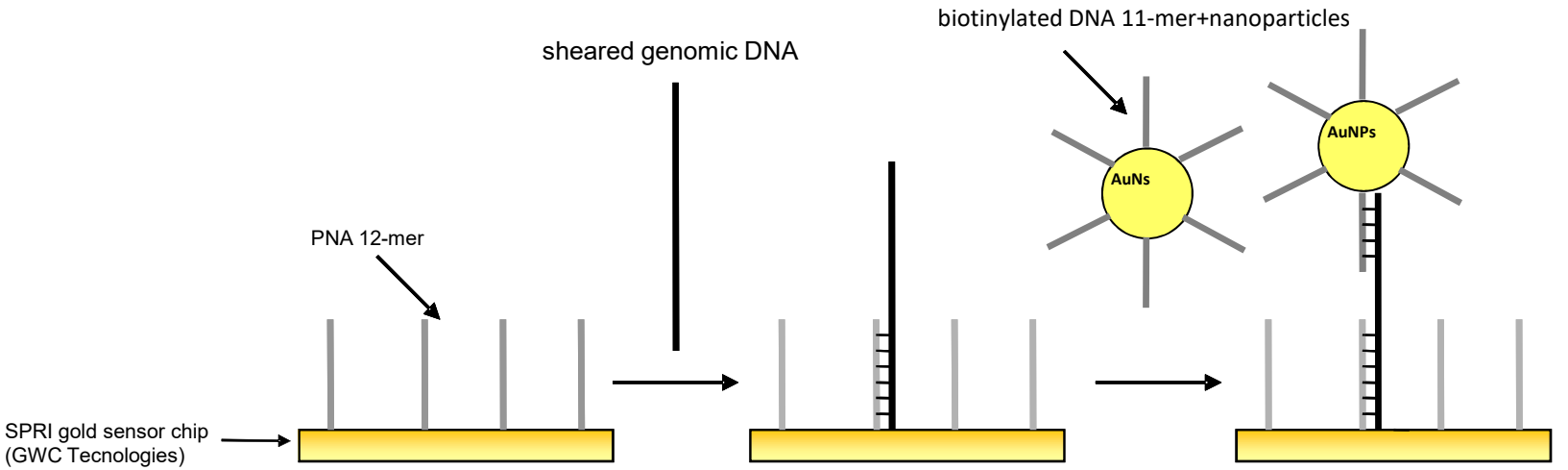
Background

D'Agata R, Breveglieri G, Zanoli LM, Borgatti M, Spoto G, Gambari R.

Direct detection of point mutations in nonamplified human genomic DNA.

Anal Chem. 2011 Nov 15;83(22):8711-7. doi: 10.1021/ac2021932. Epub 2011 Oct 21.

SPR-I experiment for PCR-free genomic DNA analysis



Injected PNA concentration: 0,1µM
Flow rate: 5µl/min
Time Immobilization: 30 min

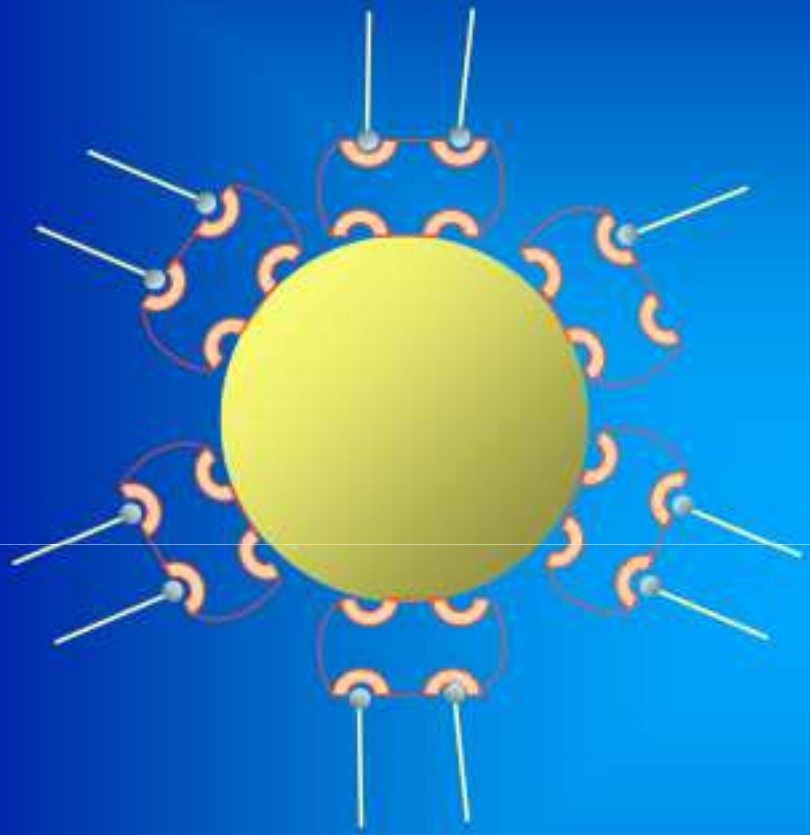
Final PNA surface coverage:
$3x10^{12}$ molecules cm-2

Injected DNA concentration: 5 pg/mL
Flow rate: 10µl/min
Time hybridization: 30 min

Biotinylated probe concentration: 1 nM (80-160 immobilized molecules/nanoparticle)
Gold nanoparticles concentration:0,1 nM
Flow rate: 15µl/min
Time hybridization: 30 min

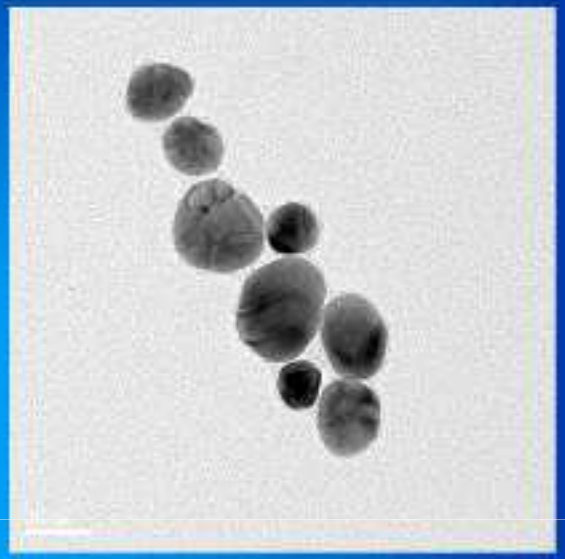
- Functionalization of SPRI gold chip (GWC Technologies) using Lomant's reagent
- Preparation of modified gold nanoparticles by sodium citrate reduction
- Microfluidic device production by replica molding technique
- Preparation of sheared genomic DNA (genomic DNA is fragmented by sonication and before analysis is boiled and cooling on ice immediately)

Gold nanoparticles

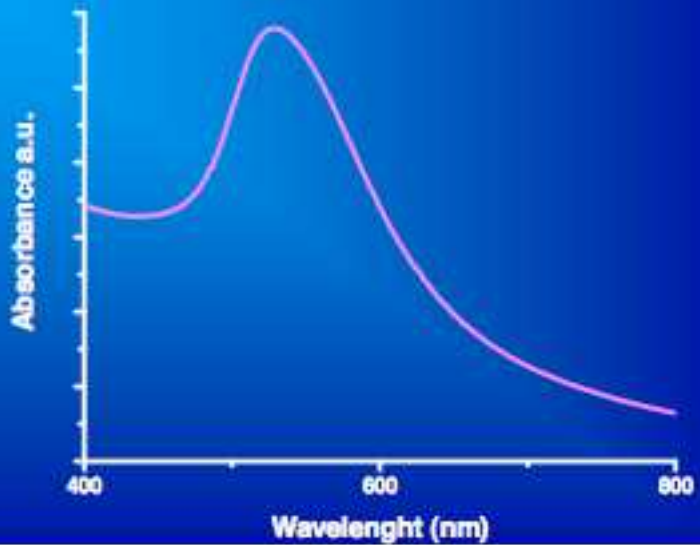


Streptavidin

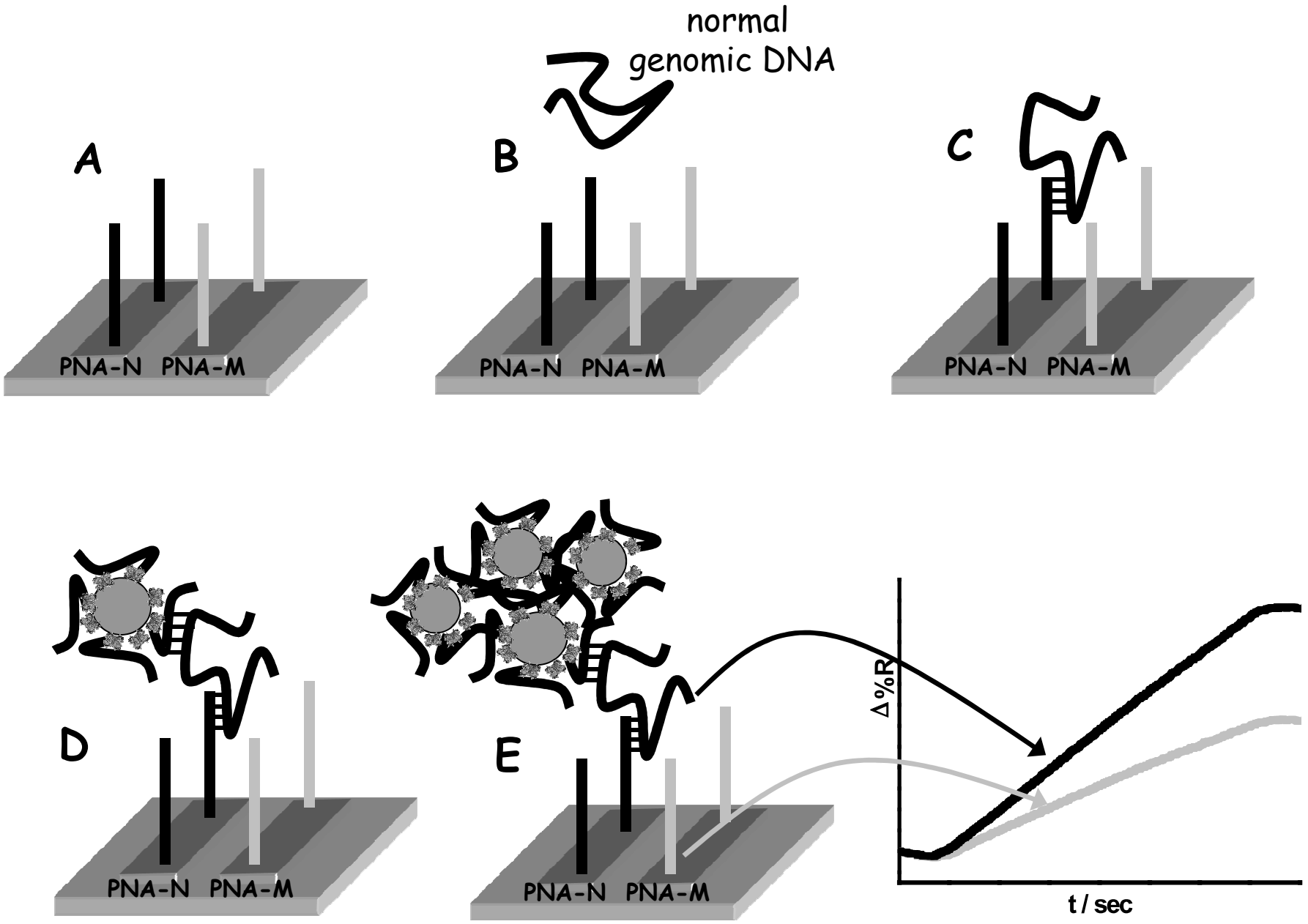
5'-GCAGCTTATCGT-3'-Biotin



d=20 (±5) nm



K. C. Grabar et al. *Anal. Chem.* 1995.67. 735-743
L. He et al. *J. Am. Chem. Soc.* 2000. 122. 9071-9077


normal
genomic DNA
A
B
C
PNA-N PNA-M
PNA-N PNA-M
PNA-N PNA-M
D
E
PNA-N PNA-M
PNA-N PNA-M
Δ%R
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ULTRAsensitive PLAsmonic devices for early CAncer Diagnosis

- Type of Action: Research and Innovation Actions
- Focus area: Personalising Health and Care
- Call: H2020-PHC-2014-two-stage
- Topic: PHC-10-2014: Development of new diagnostic tools and technologies: in vitro devices, assays and platforms
- Stage 1: 11 March 2014; proposals: 462
- Stage 2: 19 August 2014; proposals: 132
- Maximum EU Grant amount: 6.026.456 €
- Start date: 01/05/2015
- Duration: 42 months
- Grant Agreement no.: 633937

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The consortium

National Institute of Biostructures and Biosystems (Univ. Catania – Coord., Univ. Firenze, Univ. Parma)	IT	RTD
Austrian Institute of Technology	AT	RTD
Institute of Photonics and Electronics	CZ	RTD
University of Twente	NL	UNI
University of Siegen	DE	UNI
University of Ferrara	IT	UNI
VTT Technical Research Centre of Finland	FI	RTD
Italian National Cancer Institute Regina Elena	IT	HSP
Scriba Nanotecnologie	IT	SME
Ginolis Oy	FI	SME
Future Diagnostics Solutions	NL	SME
Horiba Jobin Yvon SAS	FR	IND
Amires s.r.o.	CZ	SME

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Early diagnosis and personalized cancer treatment: bottlenecks

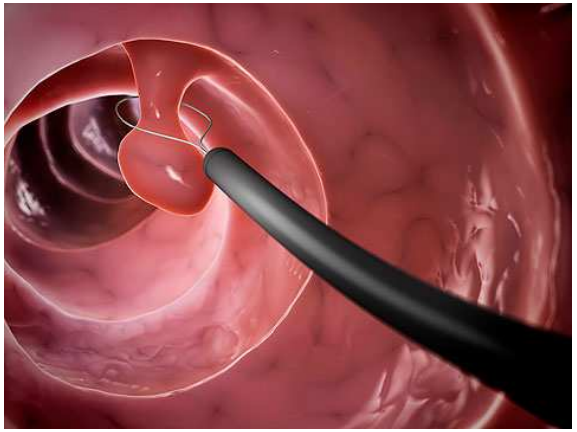
Biomarkers (companion diagnostics)

Cost

Easy and timely access to diagnostics

Gold standard: tissue biopsy

Limitations



Invasive approach

Potential clinical complications

Snapshot:

difficulty in accounting for tumor heterogeneity

Subject to tumor accessibility and patient condition

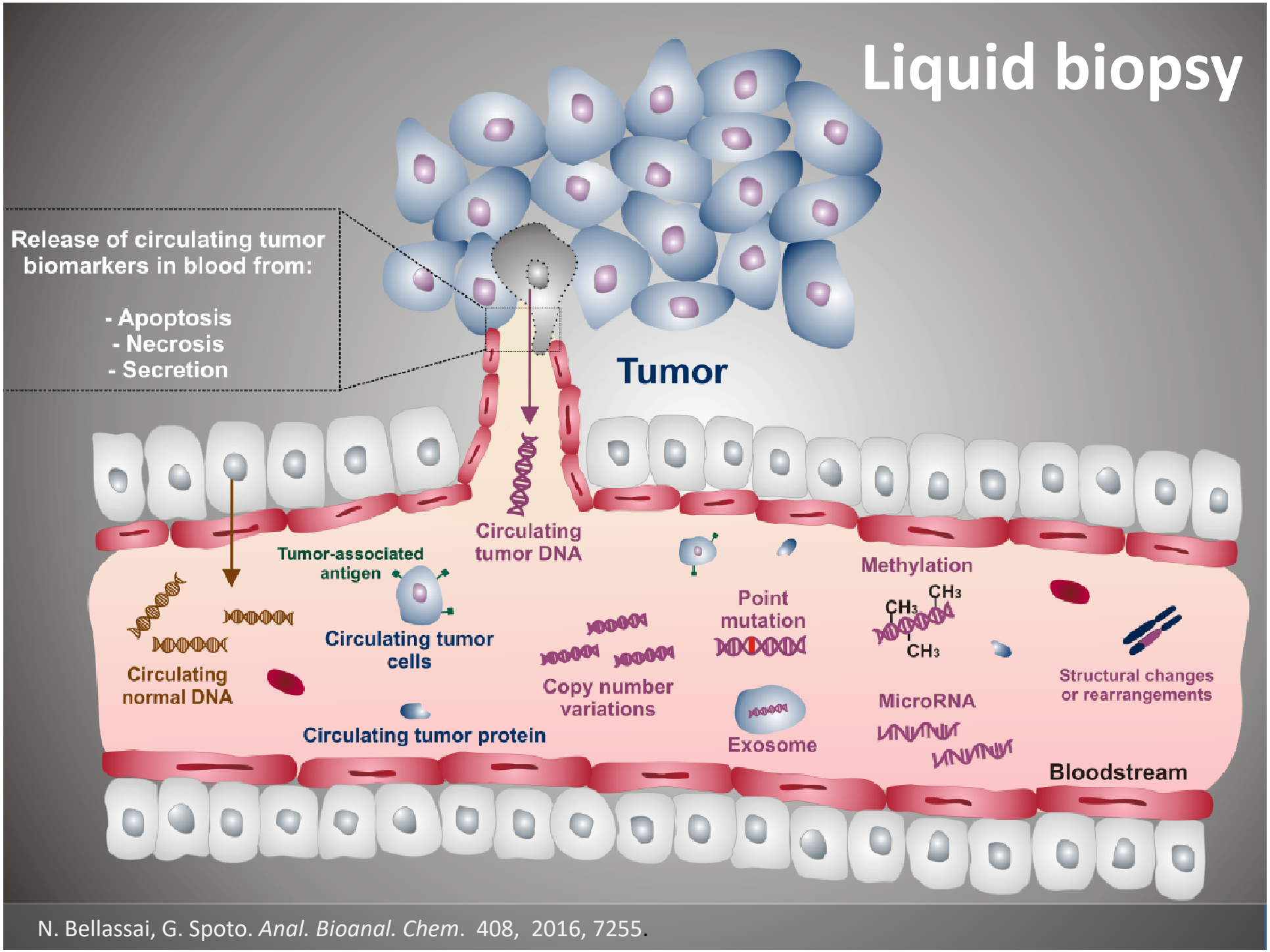
No frequent monitoring

Costly

2.6 million
breast and prostate biopsies per year in the U.S.*

*M. Denis *The Pathologist*, 6, 2015, 33.

Liquid biopsy



N. Bellassai, G. Spoto. *Anal. Bioanal. Chem.* 408, 2016, 7255.

Liquid biopsy

Advantages

Non invasive

Assesment of tumor heterogeneity

No subject to tumor accessibility and patient condition

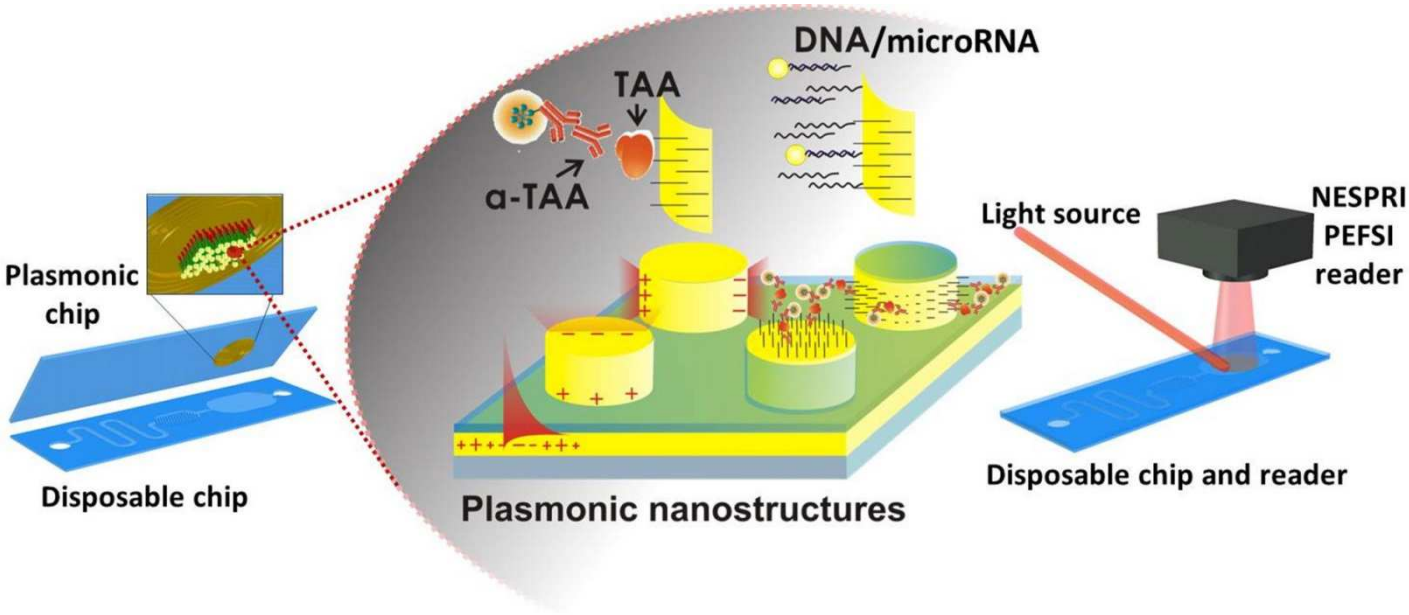
Frequent monitoring

Faster and cheaper than tissue biopsy

Crowley, E. et al. Nat. Rev. Clin. Oncol. 2013; 10:472-484

The aim

Novel in vitro diagnostic system for minimally invasive colorectal cancer early diagnosis, prognosis, patient follow-up and therapy efficacy assessment.



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Colorectal cancer in Europe

- **Second most frequent cancer**
  (471,000 in 2012) (breast cancer is the most frequent)
- **Second most common cause of death from cancer**
  (228,000 in 2012) (lung cancer is the most common)
- **Equal distribution among women and men**
  (Incidence: 255,000 male, 216,000 women.
  Mortality: 120,000 male, 108,000 women).
- **Responsible for more than 10% of all cancer deaths**
  and for 3% of all deaths within the Europe

Colorectal cancer diagnosis and prognosis

- **Actionable biomarkers**

  DNA: all-RAS mutations

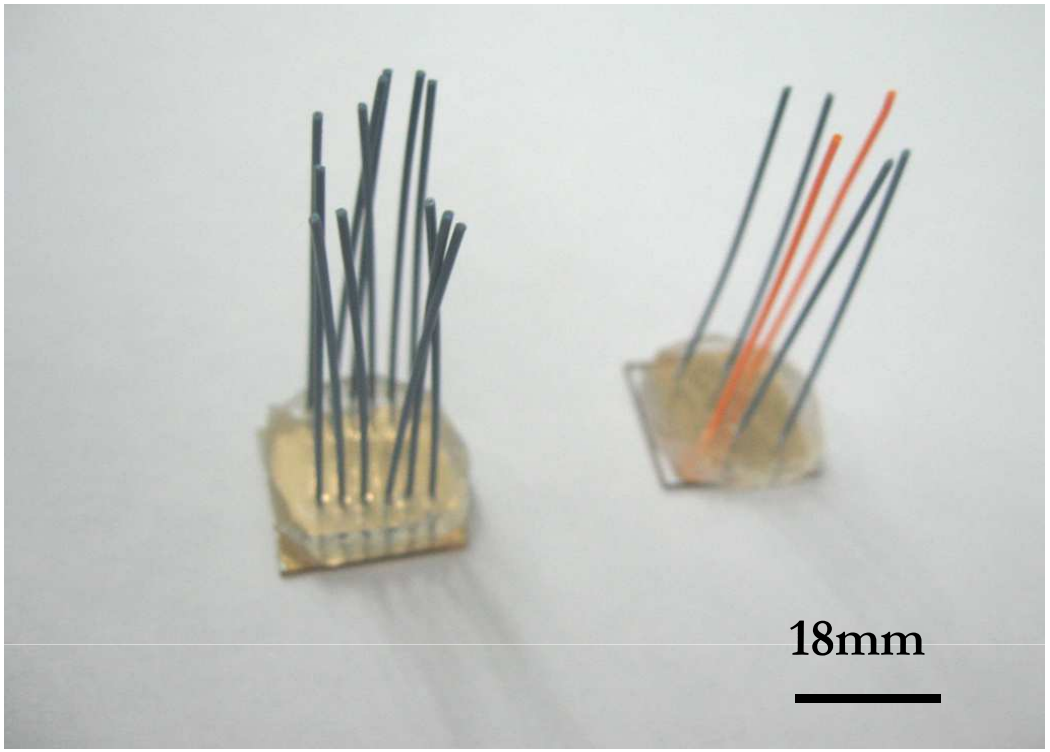
  (standard biomarkers for prognosis, follow-up and therapy assessment from solid tissue biopsy)

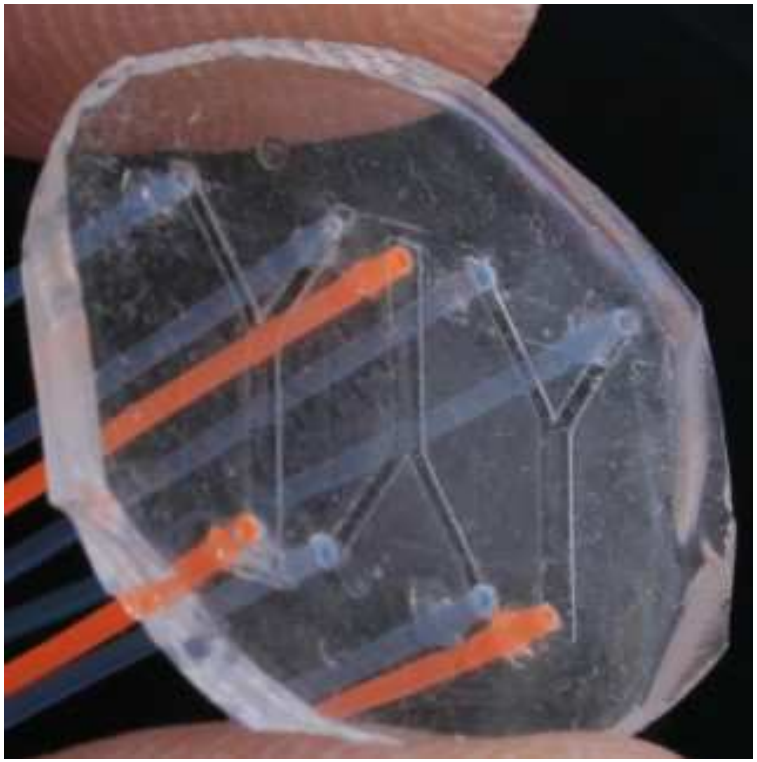
  RNA: microRNAs

  (miR-221/222, miR-141)

  Proteins: autoantibodies against tumor associated antigens

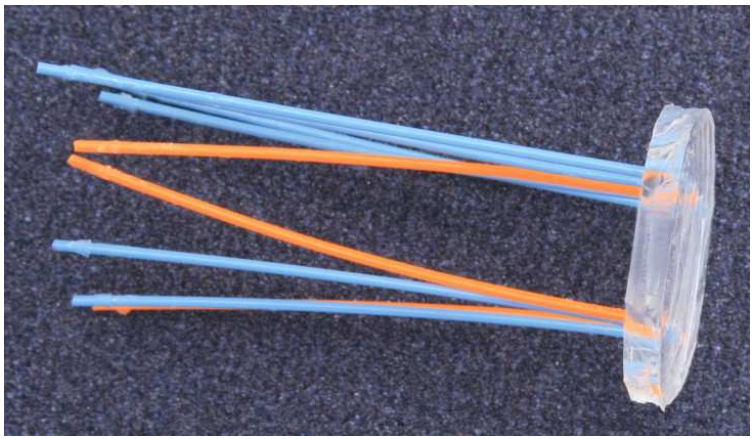
  (a-TAAs)



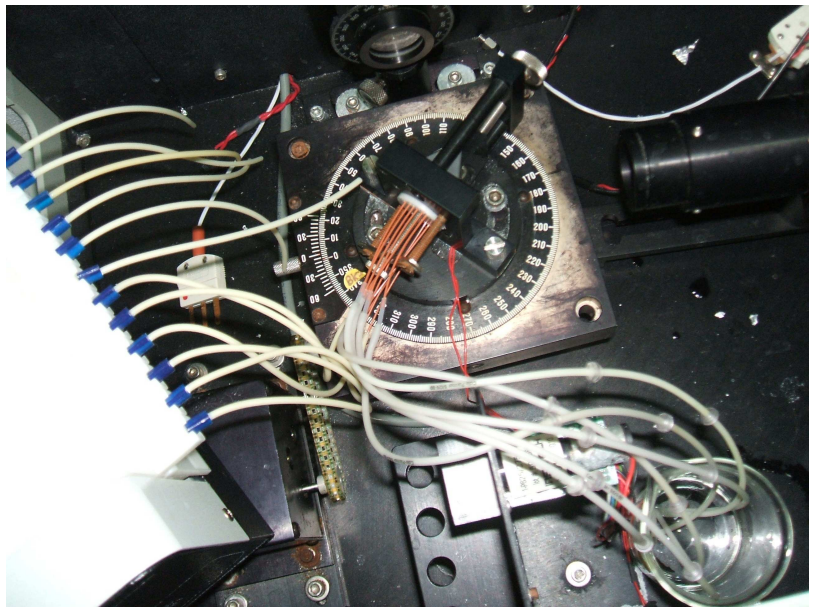


microchannels:
80 μm depth, 1.4 cm lenght,
400 μm width

circular reservoir: 400 μm



SPRI technology



Bimodal industrial prototype

Disposable chip:
low cost production

External Advisory Board

Jola Gore-Booth, Founder and Chief Executive Officer at EuropaColon

Patrice M. Milos, President and Chief Executive Officer at Medley Genomics, Providence

Maurizio Ferrari, President of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)

Markus Paulmichl, Member (Vice Chair) of the Pharmacogenomics Working Party at European Medicines Agency

David N. Reinhoudt, responsible for the Radboud Nanomedicine Alliance at Radboud University Nijmegen

Francesca Spinella, Scientific coordinator at Laboratorio GENOMA Group srl

Santiago Valor, Chief Medical Officer at SYNLAB Group, Madrid

- Stage 1: 11 March 2014; proposals: 462
- Stage 2: 19 August 2014; proposals: 132
- Funded: 9
- Final Ranking ULTRAPLACAD (unofficial): 1st

ULTRAPLACAD

AIT AUSTRIAN INSTITUTE OF TECHNOLOGY

MESA+ INSTITUTE FOR NANOTECHNOLOGY

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AMIRES

IRE ISTITUTO NAZIONALE TUMORI REGINA ELENA ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

future diagnostics

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The consortium

National Institute of Biostructures and Biosystems	IT	RTD
Austrian Institute of Technology	AT	RTD
Institute of Photonics and Electronics	CZ	RTD
Italian National Cancer Institute Regina Elena	IT	RTD
University of Twente	NL	UNI
University of Siegen	DE	UNI
University of Ferrara	IT	UNI
VTT Technical Research Centre of Finland	FI	RTD
Scriba Nanotecnologie	IT	SME
Ginolis Oy	FI	SME
Future Diagnostics Solutions	NL	SME
Horiba Jobin Yvon SAS	FR	IND
Amires s.r.o.	CZ	SME

Dissemination
Burocracy
Contacts with UE

DISSEMINATION:

Research papers
Patients Associations
Clinicians
SME/Companies
Students
Society (newspapers, TV ……)

Why Scientific Publishing

is so profitable?

A triple pay system

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Scientists give their results to publishers for free

Scientists peer review manuscripts

Governments fund libraries

Publishers sell products to libraries


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regarding
Toolbox
information
factors
review
larger
programme's

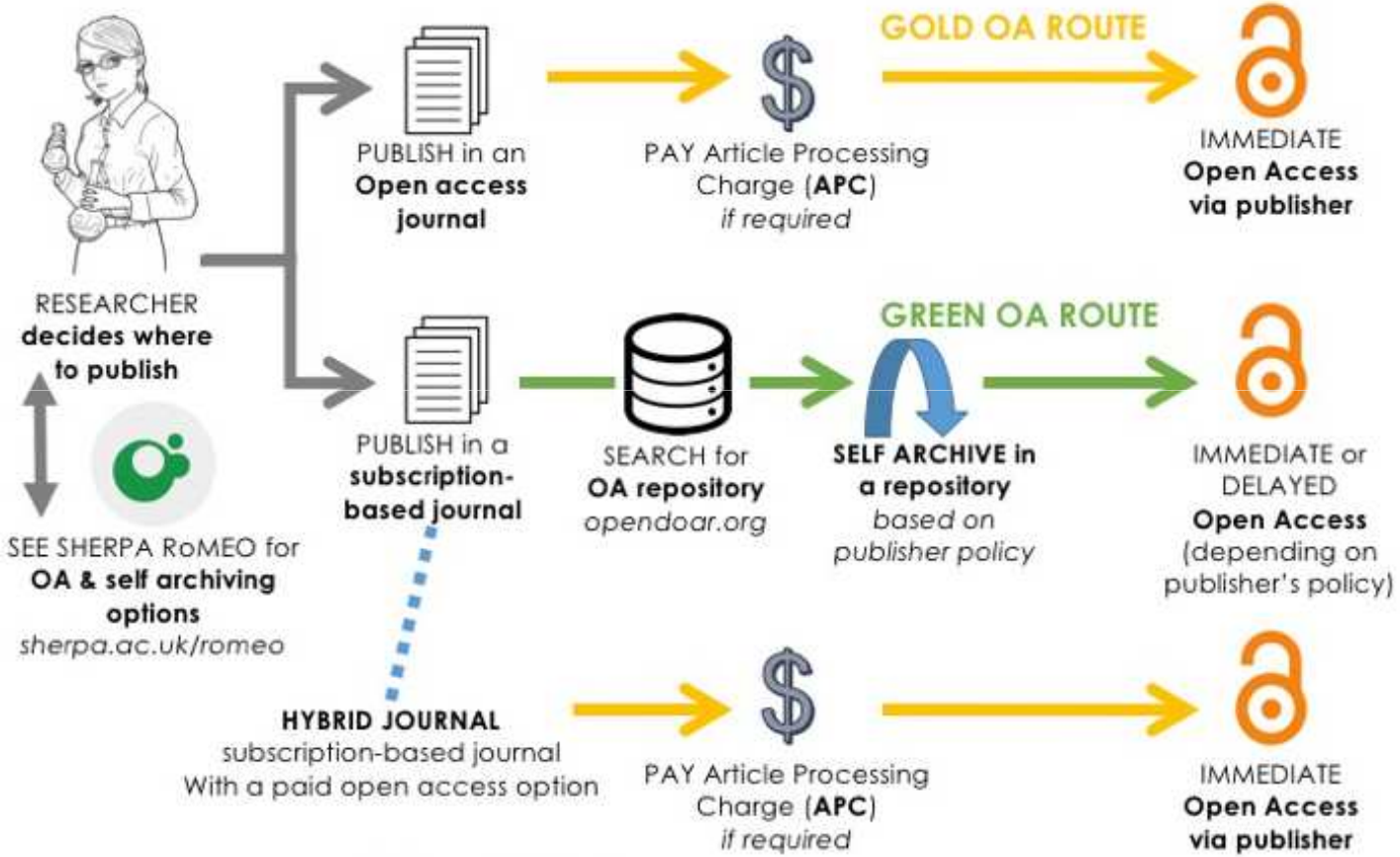
Open Access in Horizon 2020

European Commission funded projects

IN HORIZON 2020, THE EC REQUESTS ALL PROJECTS TO PROVIDE OPEN ACCESS TO ALL PEER REVIEWED ARTICLES ARISING FROM PROJECT FUNDING.

European Commission

Open Access Publishing



Darren Chase | darren.chase@stonybrook.edu Stony Brook University | Libraries

GREEN OPEN ACCESS

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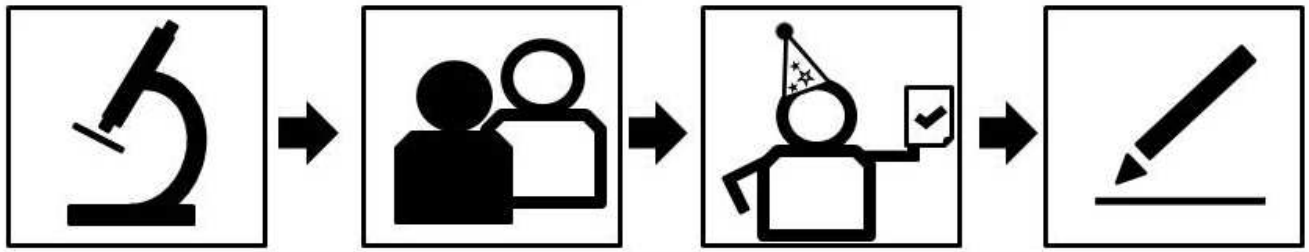

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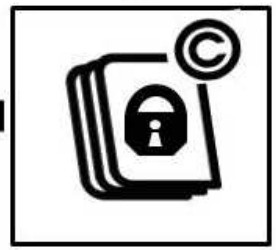

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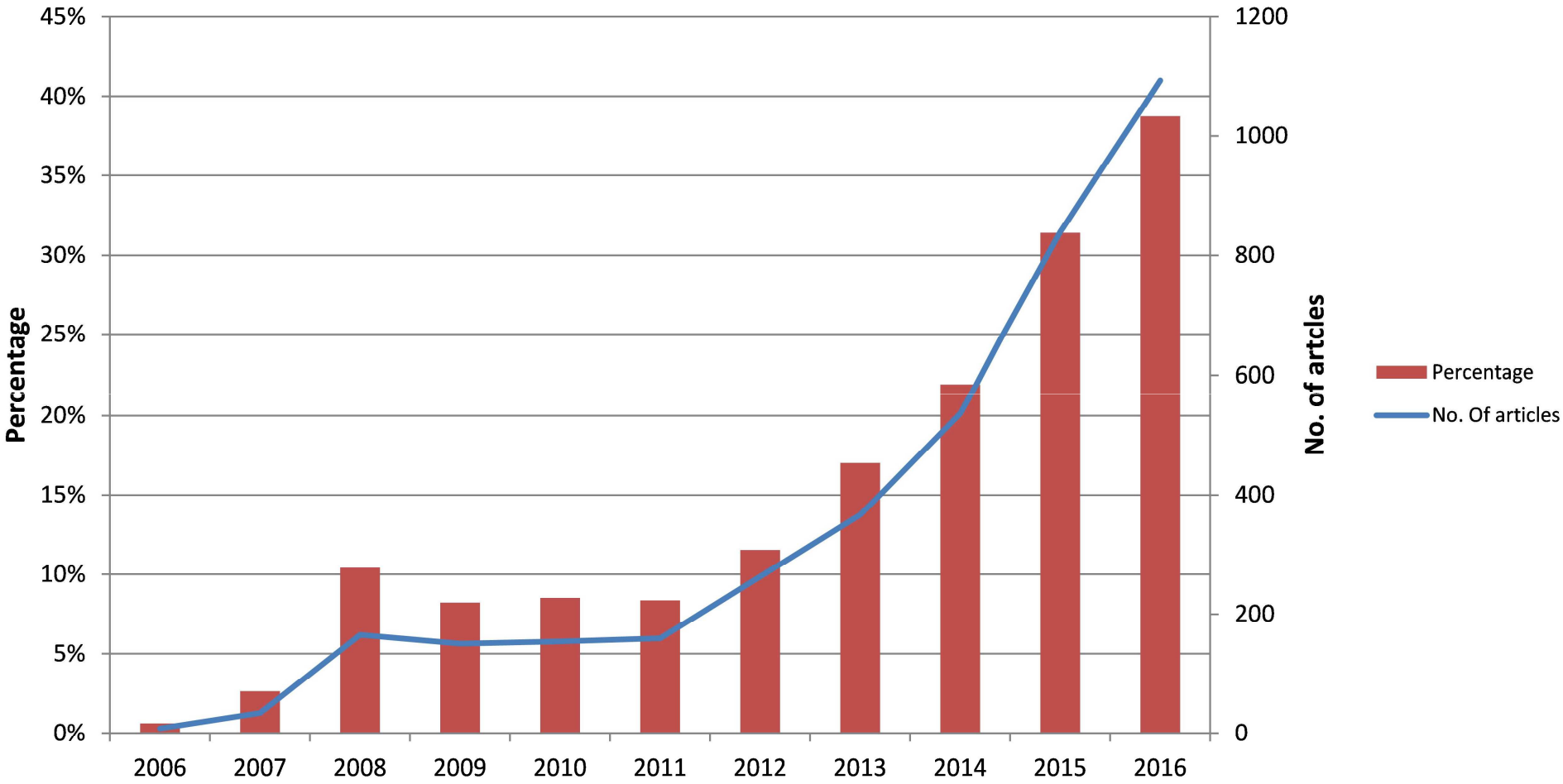
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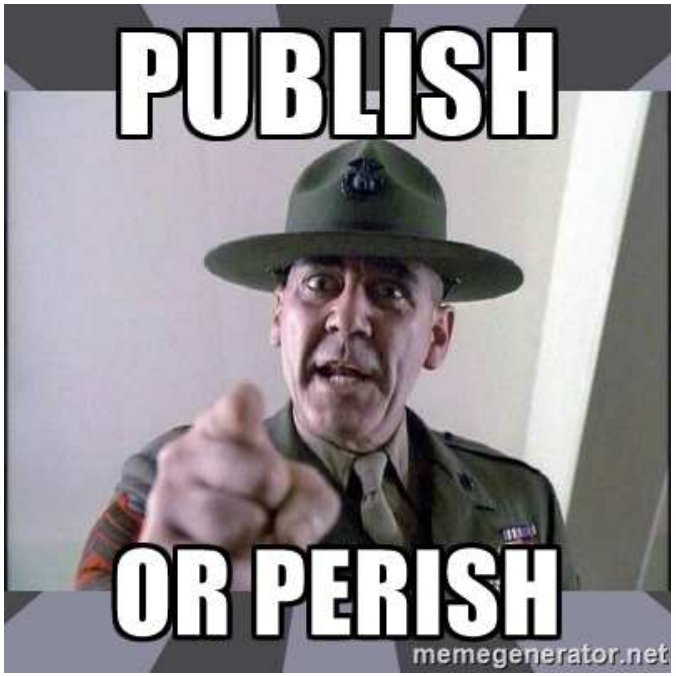
No. Of articles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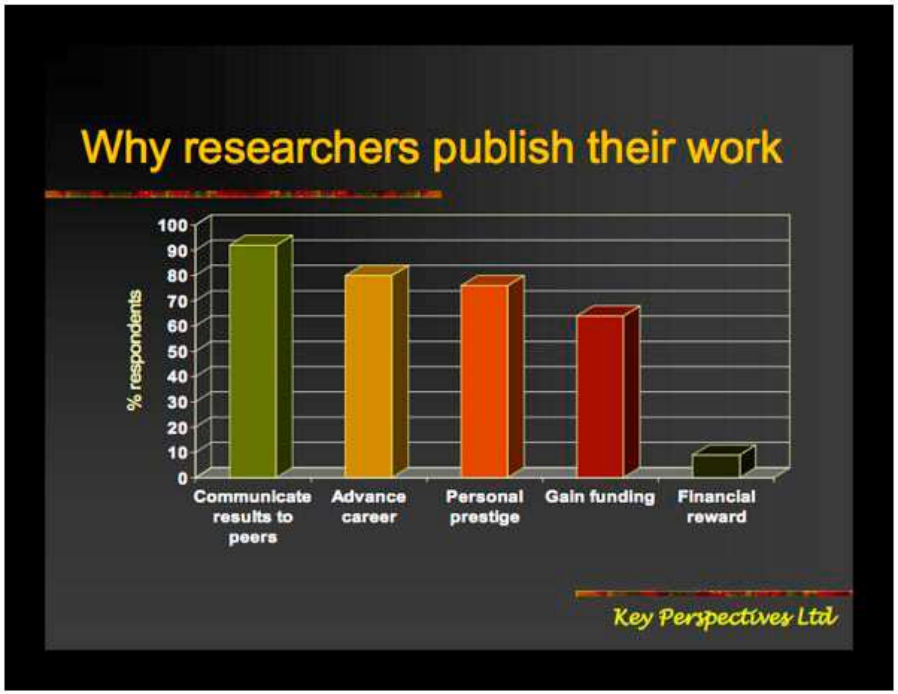
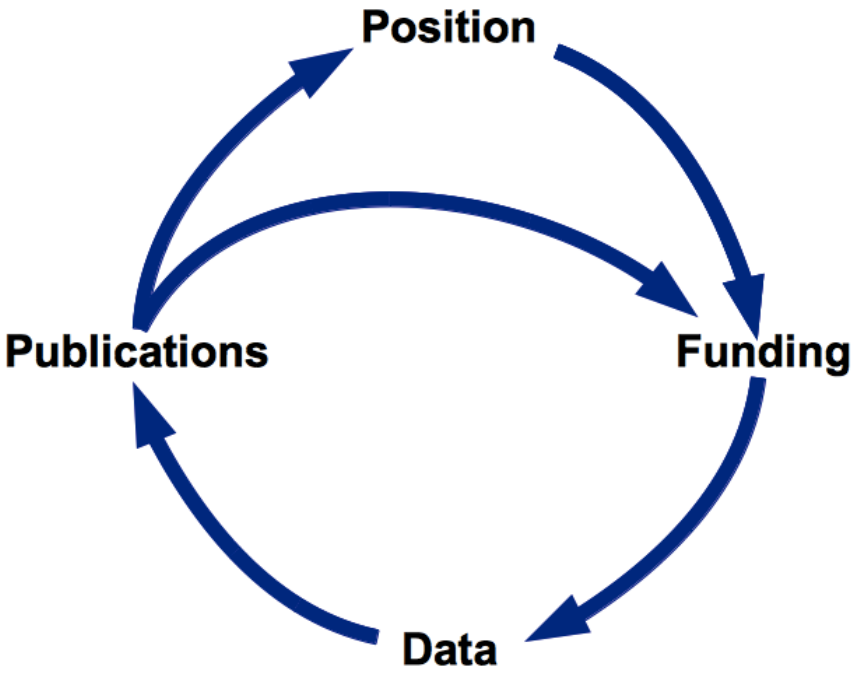
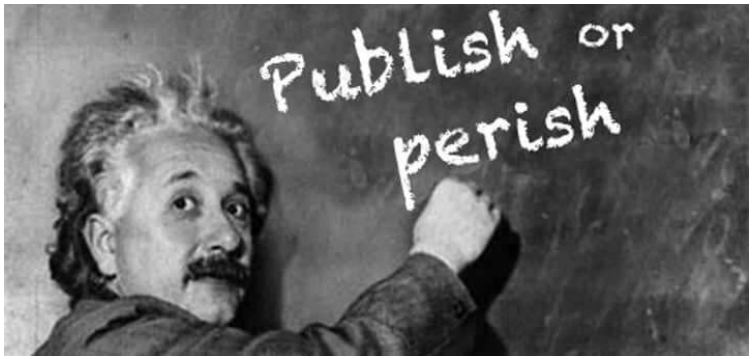
OR PERISH
memegenerator.net


Why researchers publish their work
% respondents
100
90
80
70
60
50
40
30
20
10
0
Communicate results to peers
Advance career
Personal prestige
Gain funding
Financial reward
Key Perspectives Ltd

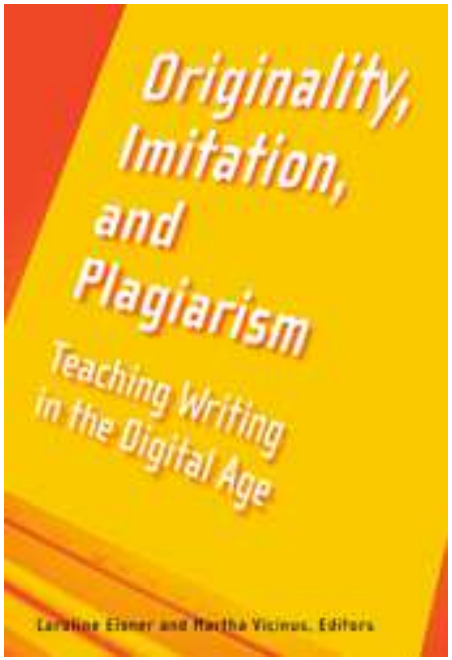

Position
Publications
Funding
Data


Publish or perish

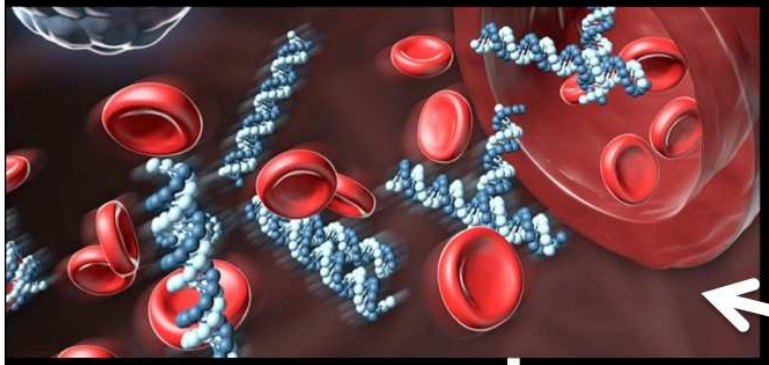
Plagiarism

- Paraphrasing an article, book or journal too closely
- Missing out punctuation in a citation
- Submitting a publication that you didn't write
- Copying words or ideas from someone else's work, without giving credit
- Giving incorrect information about the source of a quotation
- Copying sentence structure but changing words around, without giving credit
- Copying from your own work

Source: http://www.scanmyessay.com/plagiarism/what-is-plagiarism.php

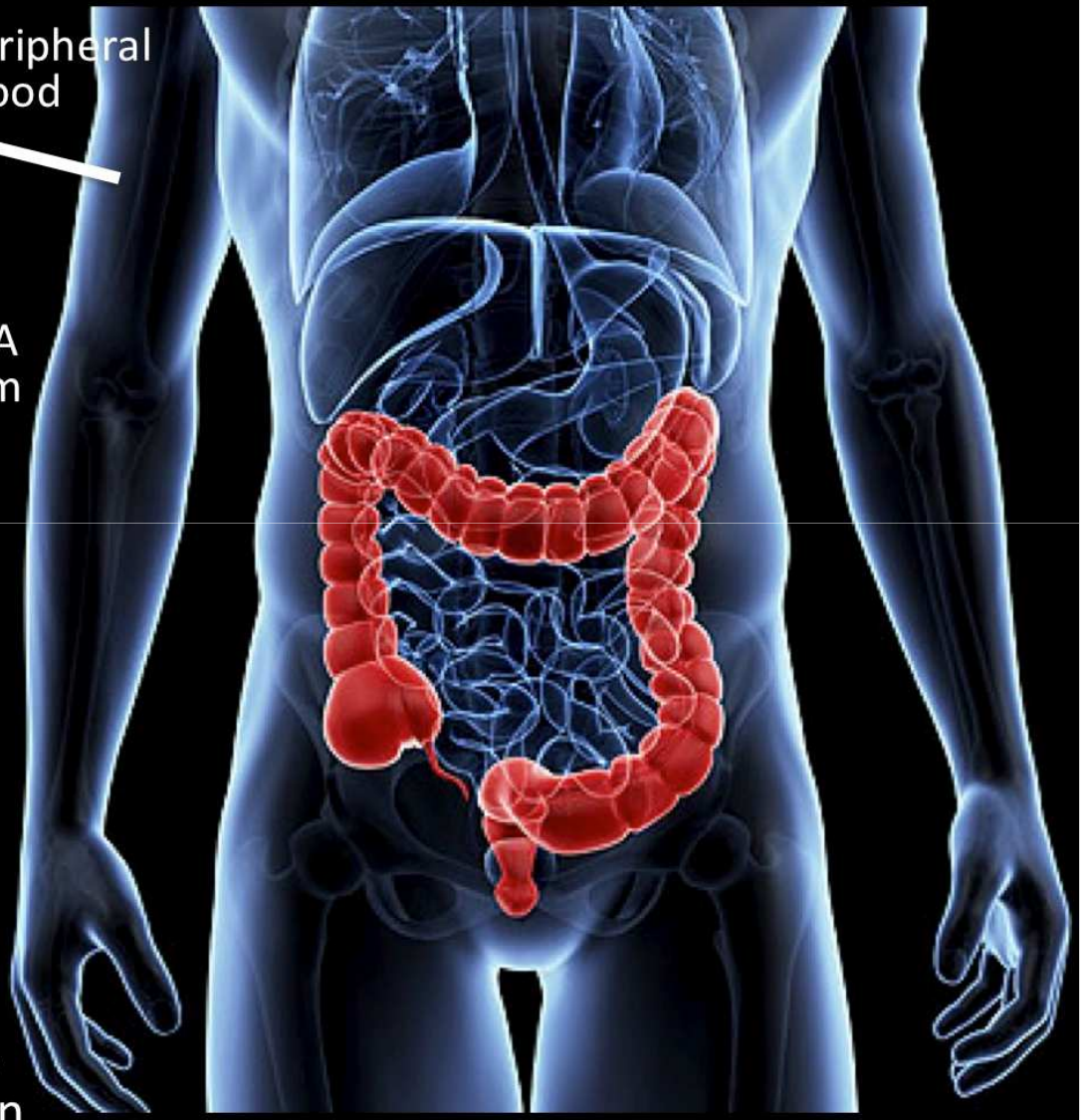


Liquid biopsy in colon cancer



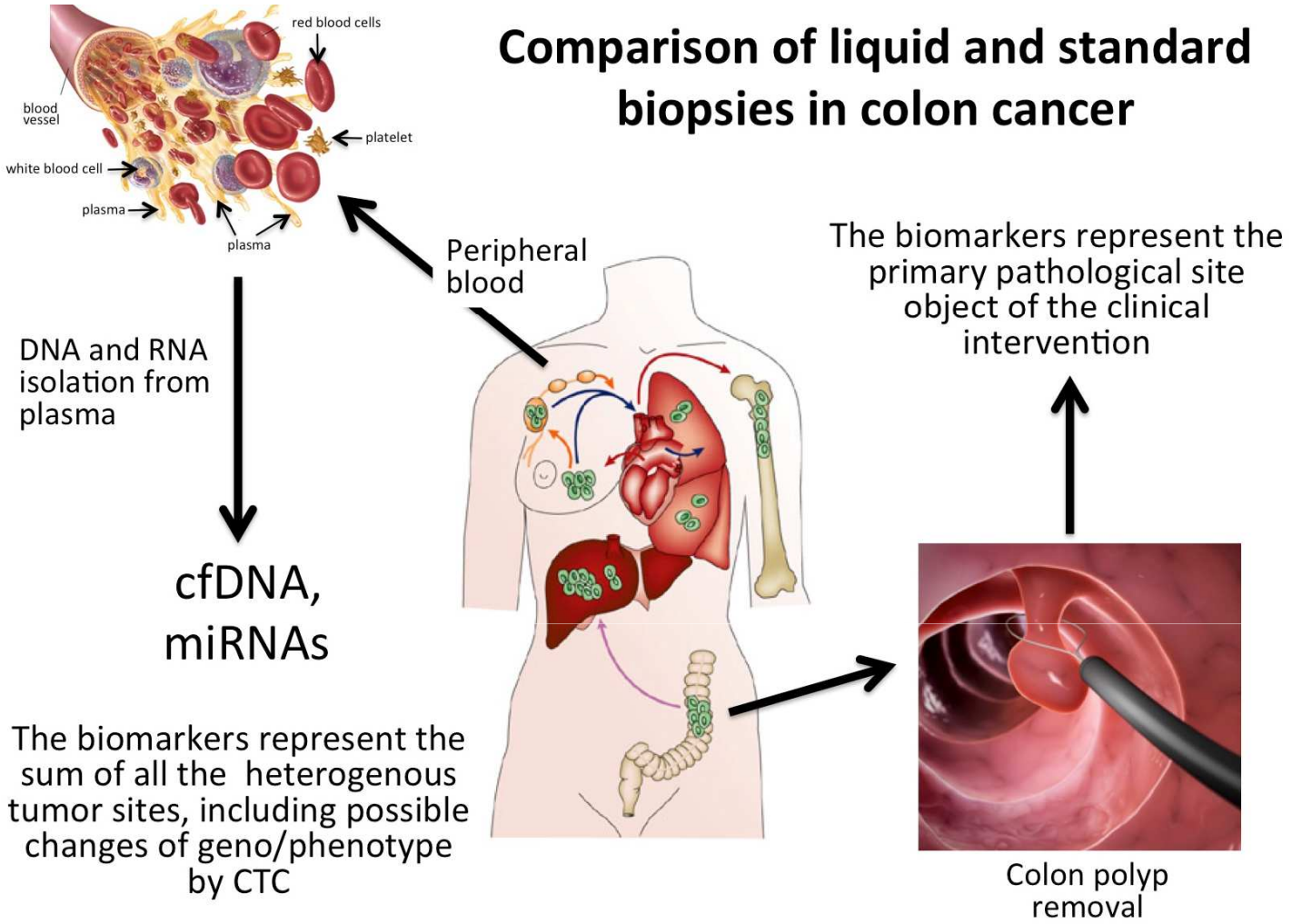
Peripheral blood

DNA and RNA isolation from plasma



cfDNA, miRNAs

- Early diagnosis
- Staging
- Prognosis
- Follow up
- Therapy outcome
- Therapy response prediction



Patrizio Giacomini - Istituto Regina Elena, Roma - 13 luglio 2017, ore 15

Liquid Biopsy in the Practice of Precision Oncology

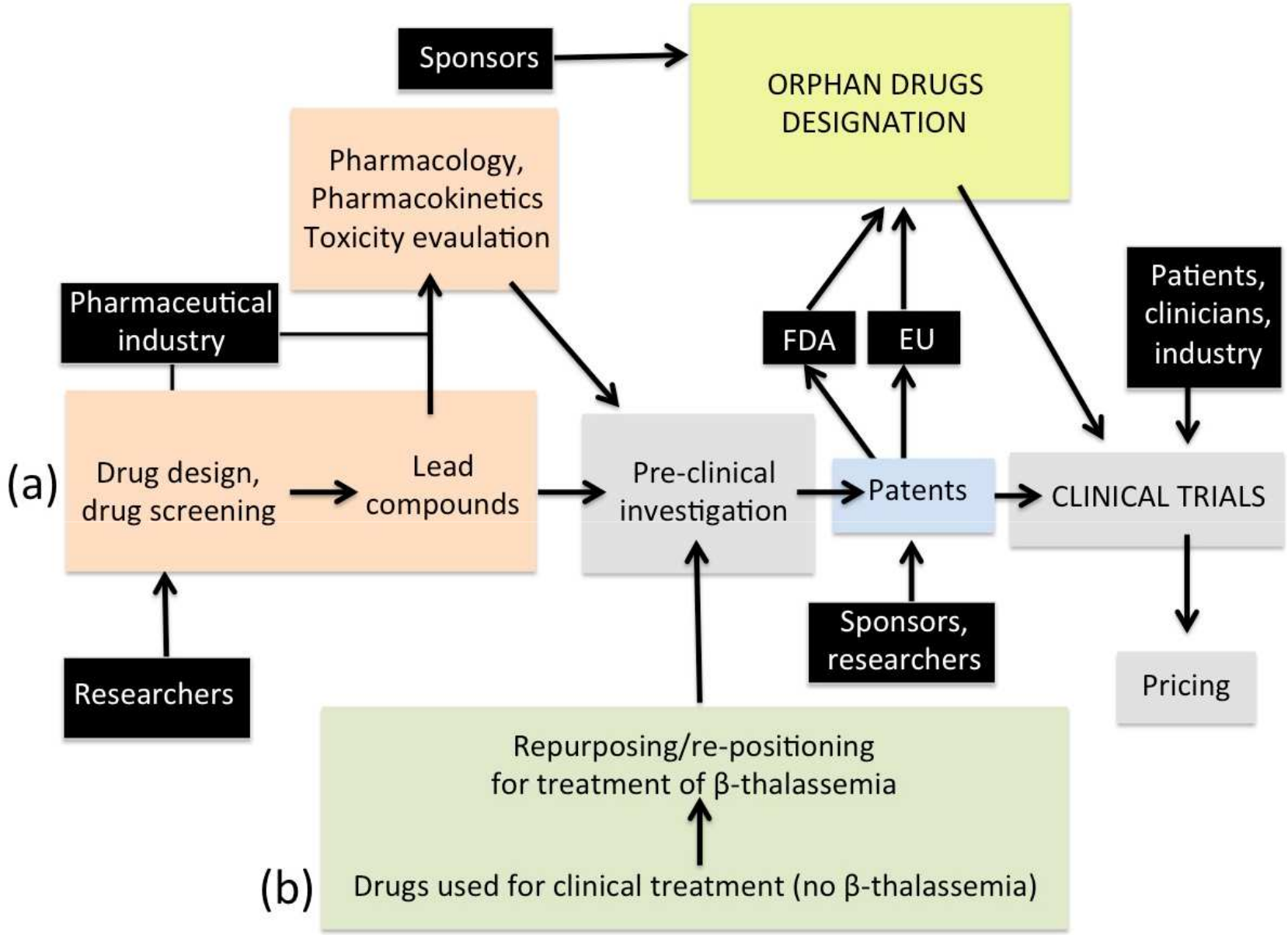
https://youtu.be/FvEVv-E-SGM

Key points sustaining projects within the Health program

- OMICS
- Personalized Therapy
- Rare diseases
- Repurpusing of drugs
- Cellular Biobanks

Orphan drug designation (EMA)

Patents



Finotti et al., Expert Opinion on Orphan Drugs, 2016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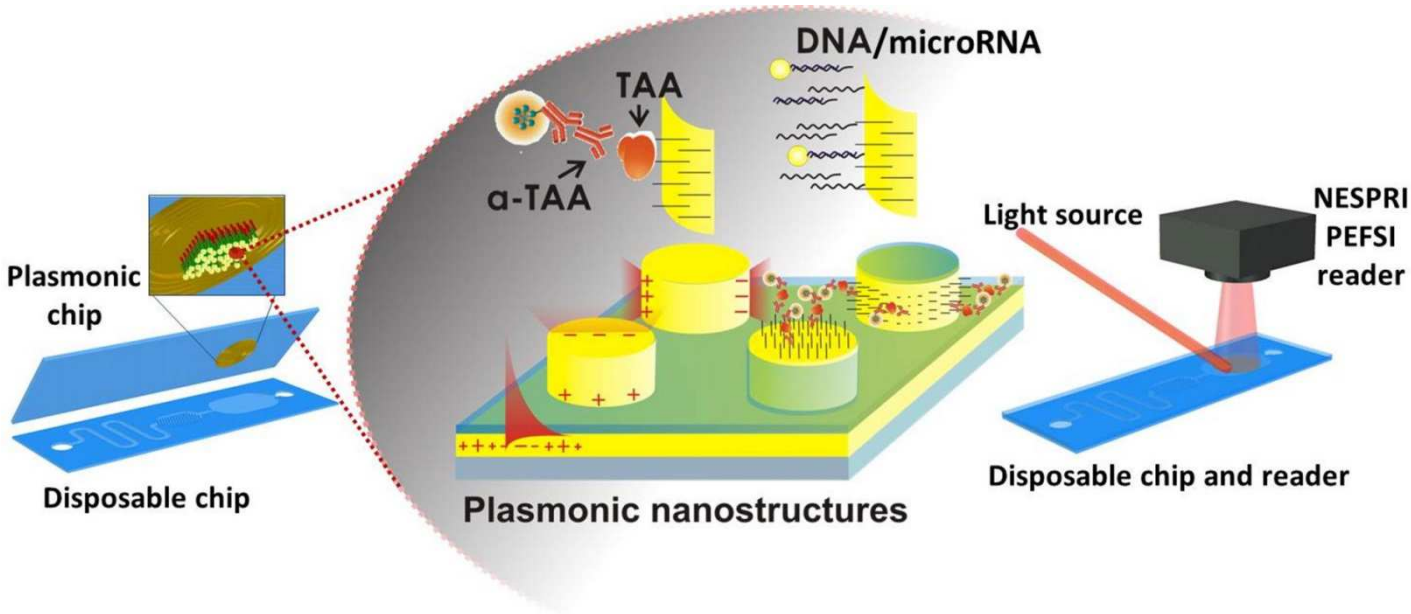
ULTRAsensitive PLAsmonic devices for early CAncer Diagnosis

Novel in vitro diagnostic system for minimally invasive colorectal cancer early diagnosis, prognosis, patient follow-up and therapy efficacy assessment.



NESPRI: Nanoparticle-enhanced surface plasmon resonance imaging: DNA and microRNAs

PEFSI: Plasmon-enhanced fluorescence spectroscopy imaging : a-TAAs

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THE FRAMEWORK PROGRAMME FOR RESEARCH AND INNOVATION
HORIZON 2020

Good luck!!!!