



THERABOT

Therapeutic Bacteria Biohybrids for Oncology Treatment

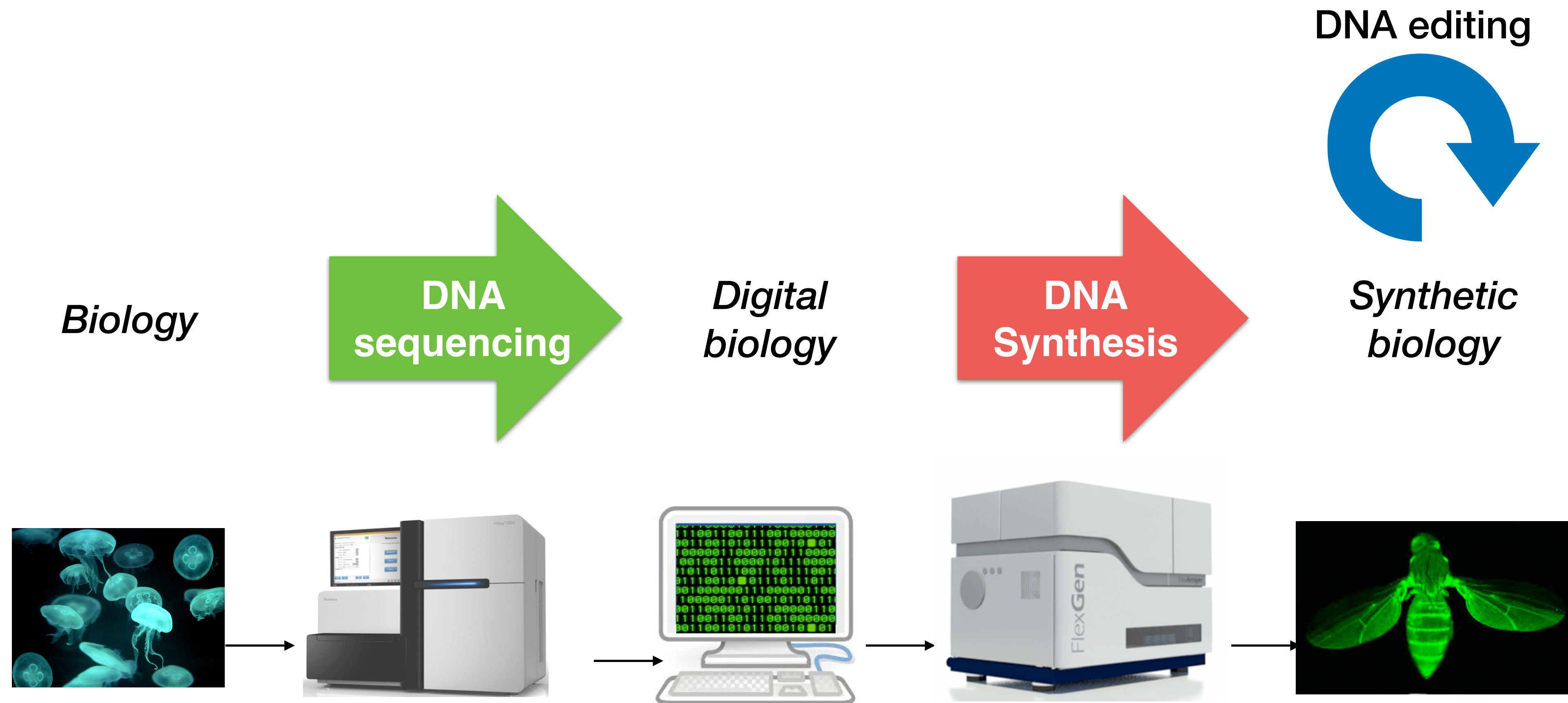
MARIE SKŁODOWSKA-CURIE ACTIONS
Staff Exchanges (SE)

Diego CATTONI
Synthetic Biology Team
Centre de Biologie Structurale

MSCA
Marie Skłodowska-Curie Actions
Developing talents, advancing research

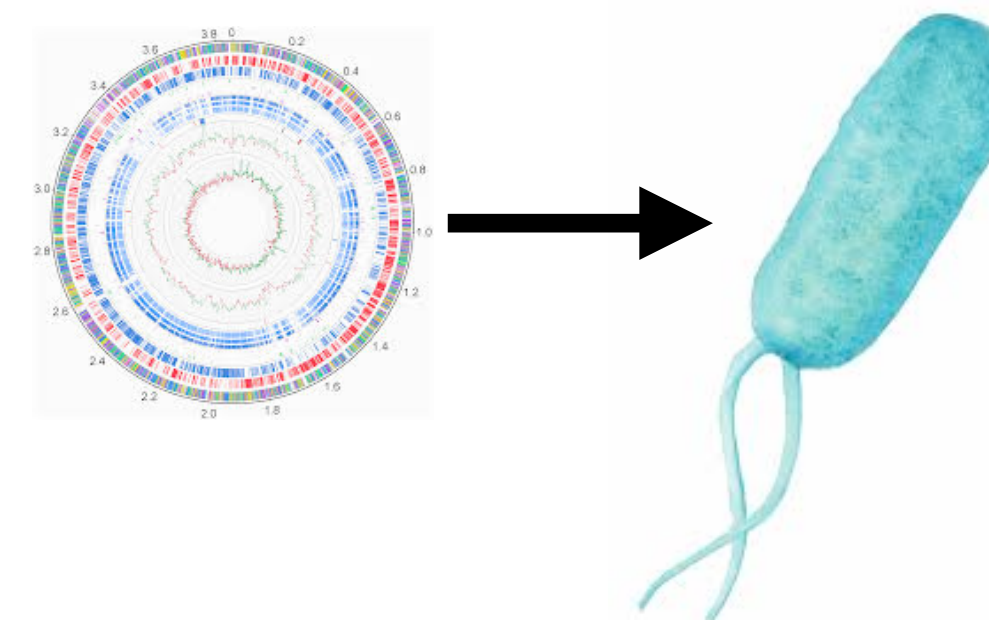
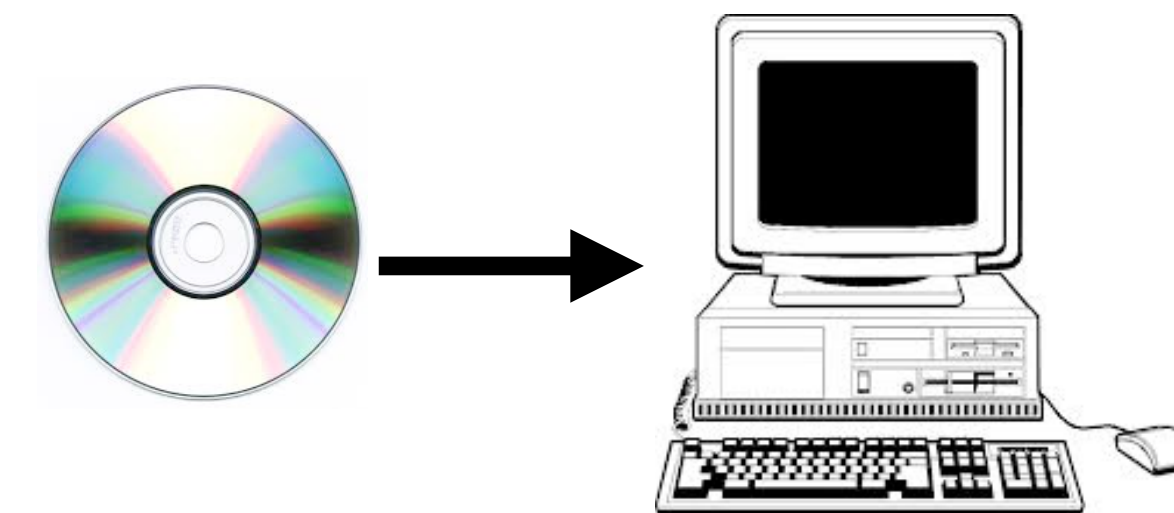
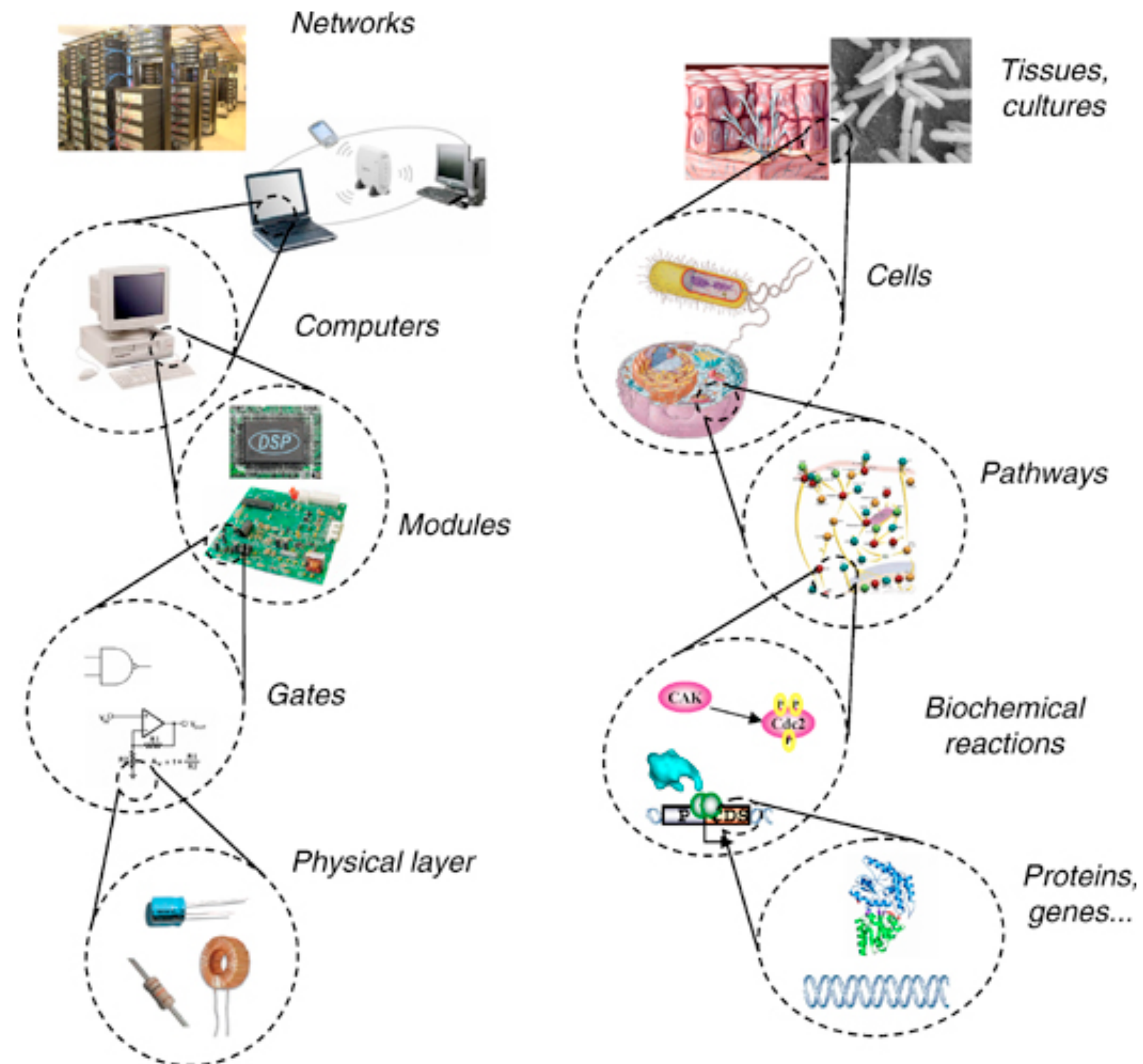


Synthetic biology: engineering new biological systems and functions

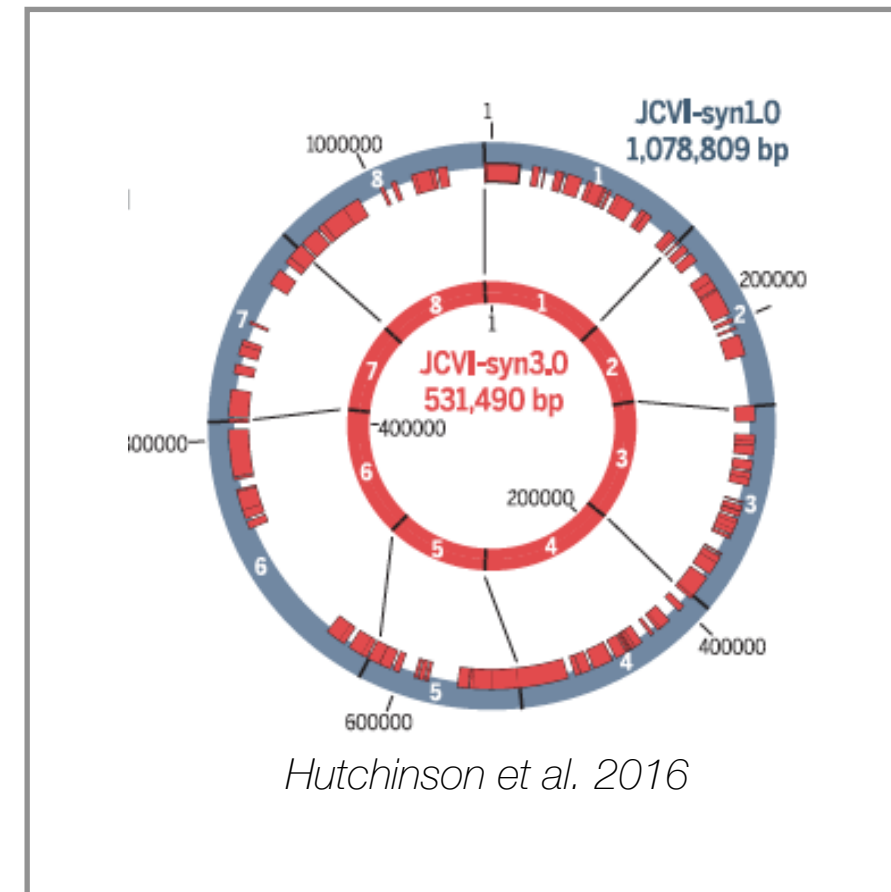
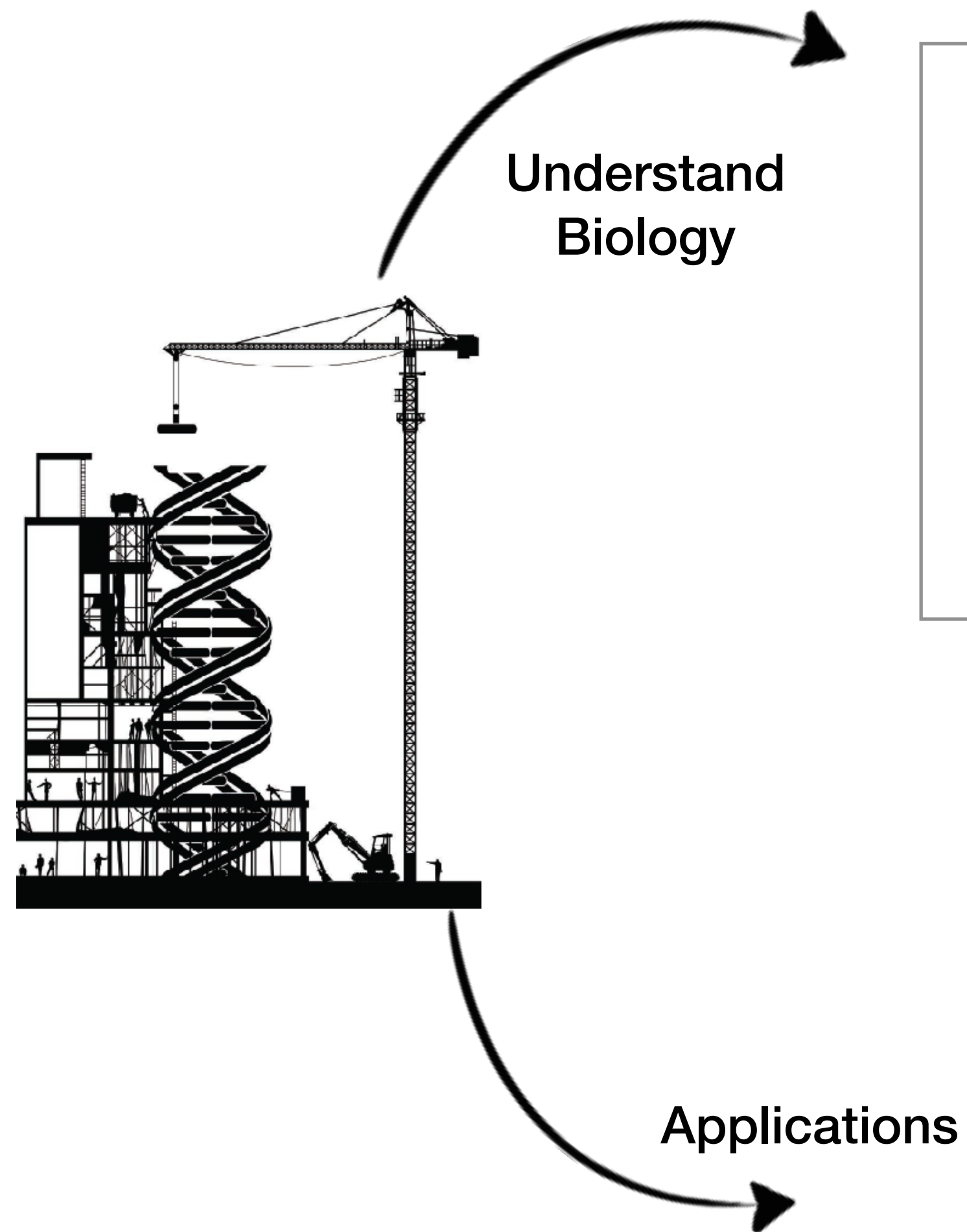


Synthetic biology: engineering new biological systems and functions

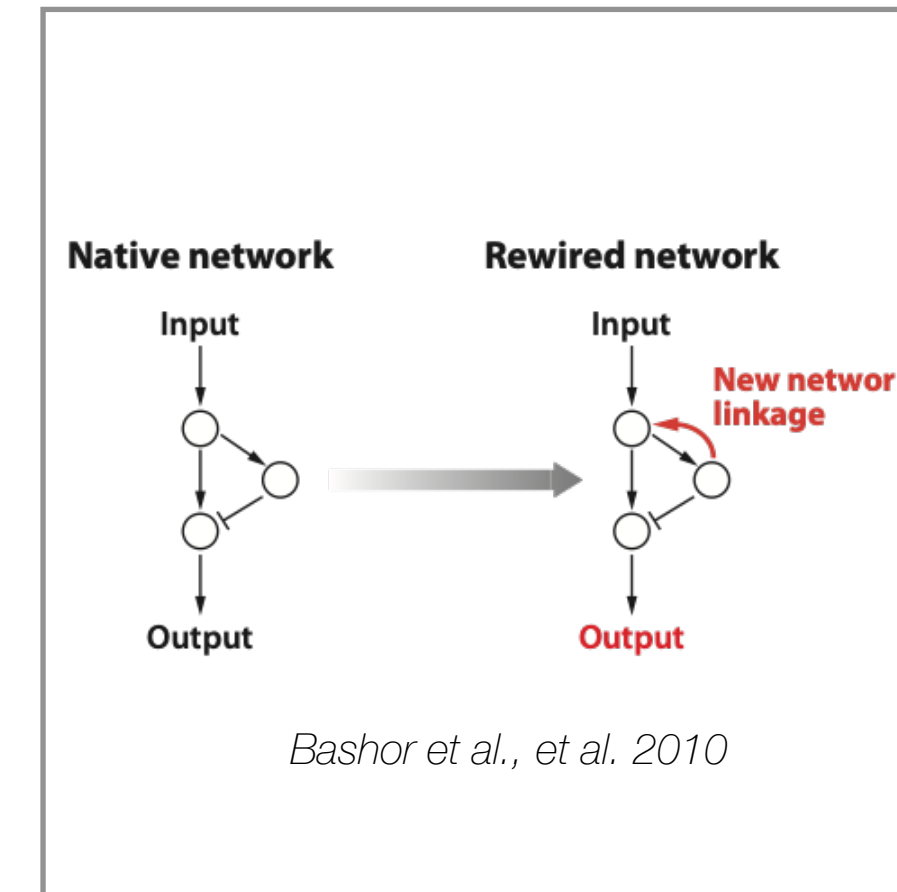
Inspirations: mature engineering sciences (electronics)



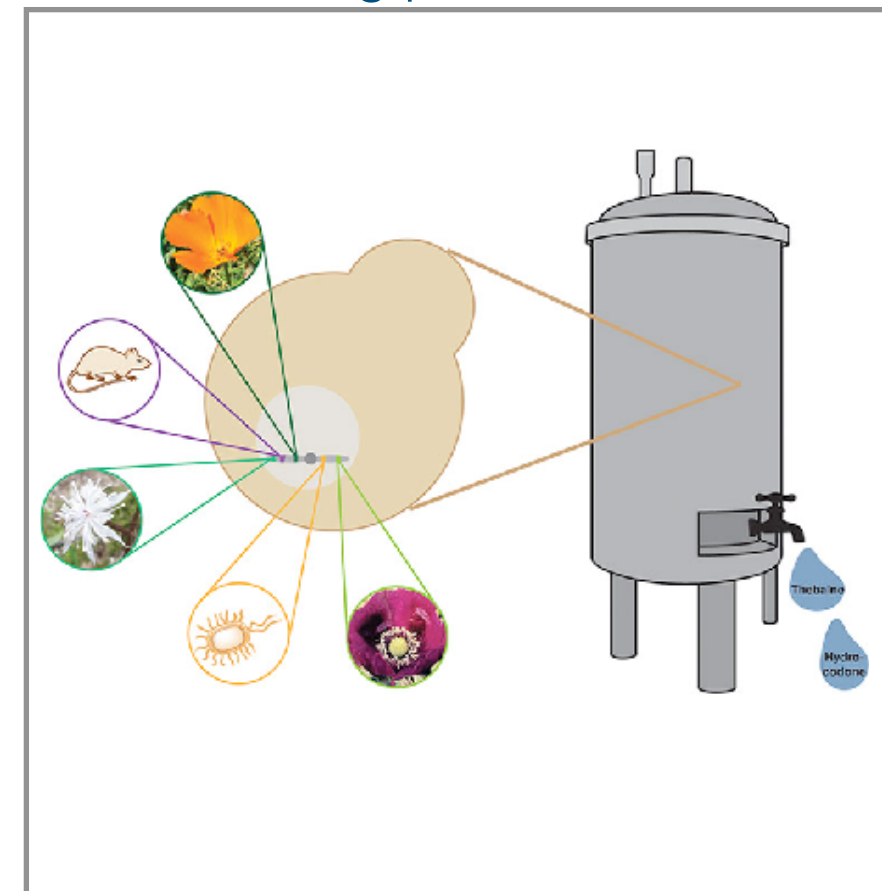
Synthetic biology: engineering new biological systems and functions



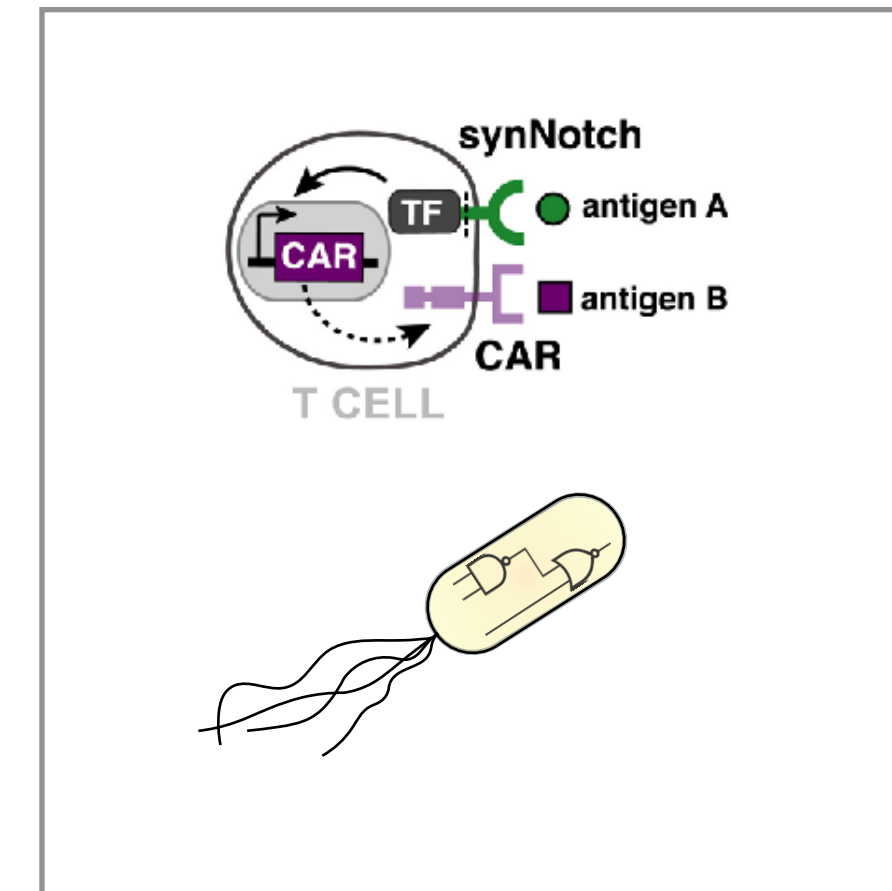
Synthetic genomes



Synthetic signaling

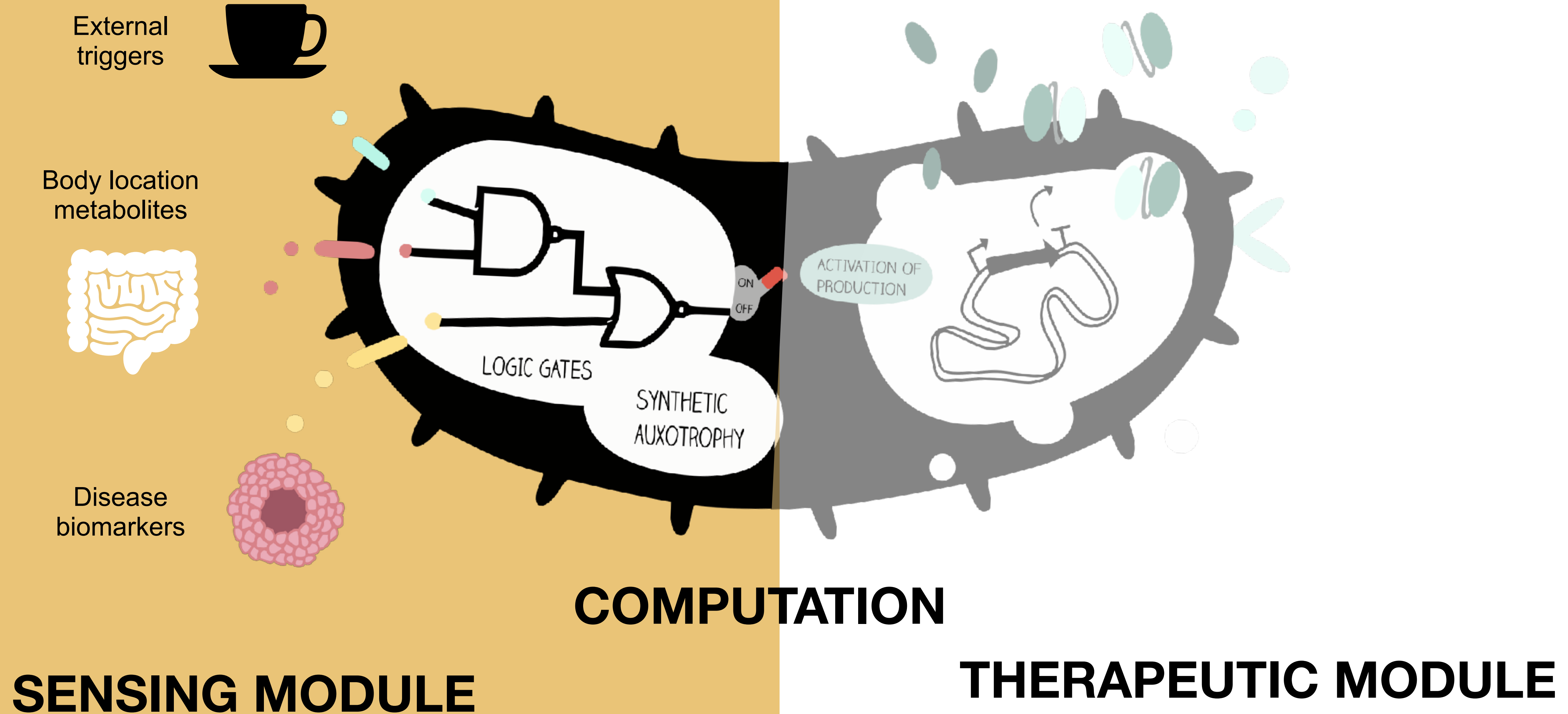


Galanie et al. 2016

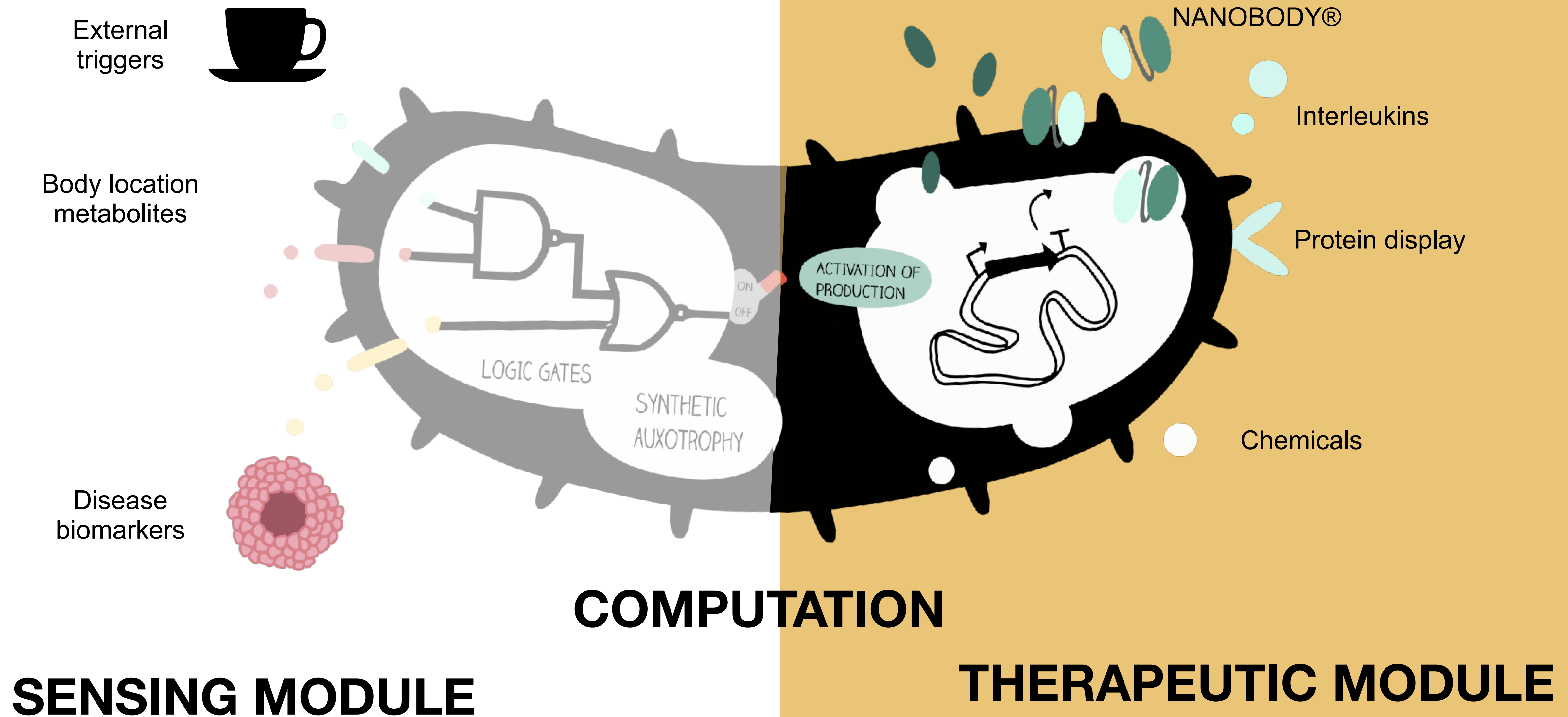


Roybal et al. 2016

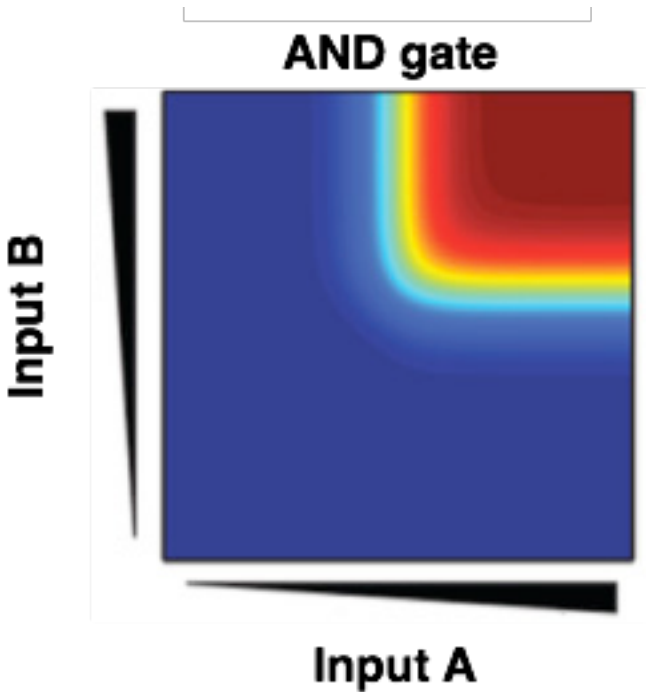
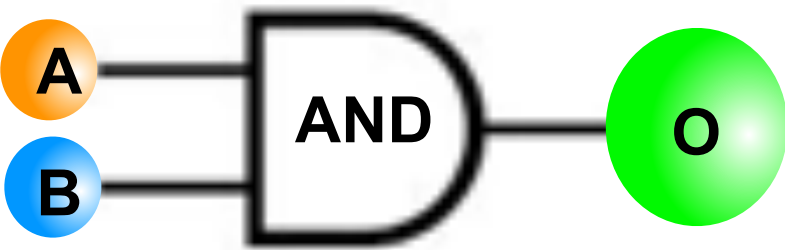
Integrated sensing and computing for therapeutic bacteria



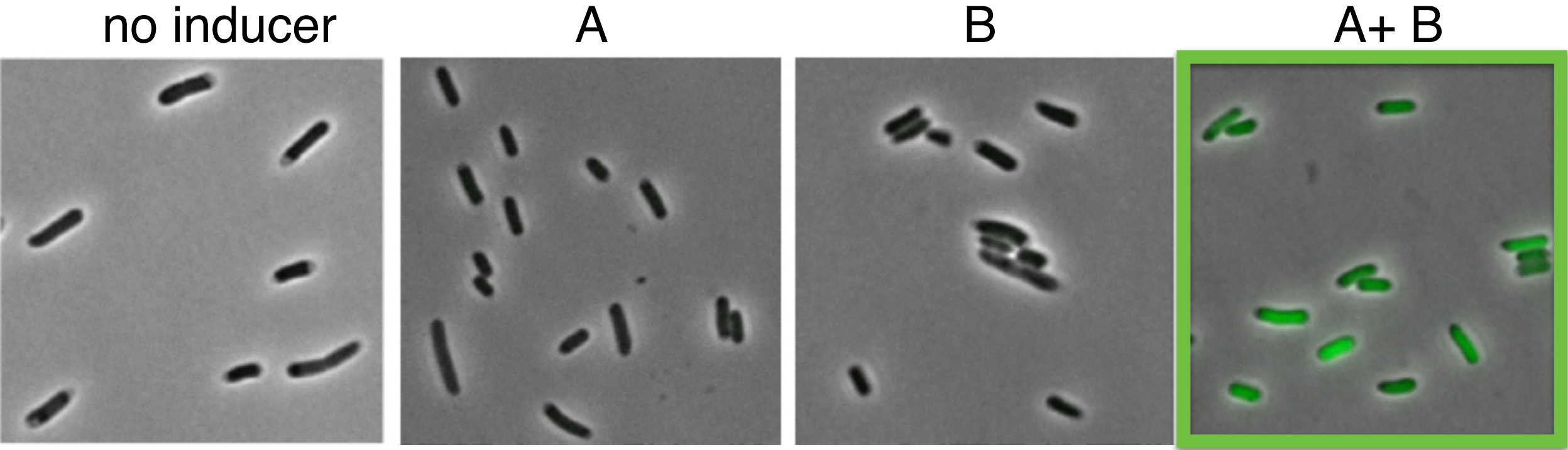
Integrated sensing and computing for therapeutic bacteria



Engineering biological logic gates

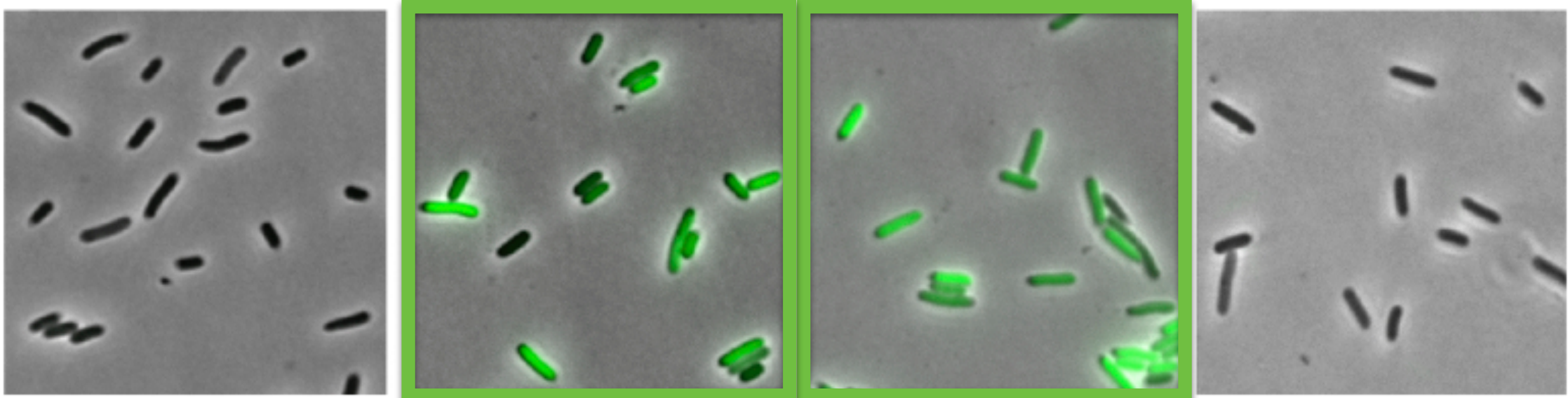


AND



A	B	Output
0	0	0
0	1	0
1	0	0
1	1	1

XOR



A	B	Output
0	0	0
0	1	1
1	0	1
1	1	0

The global cancer burden

Incidence

Cases
19 976 499

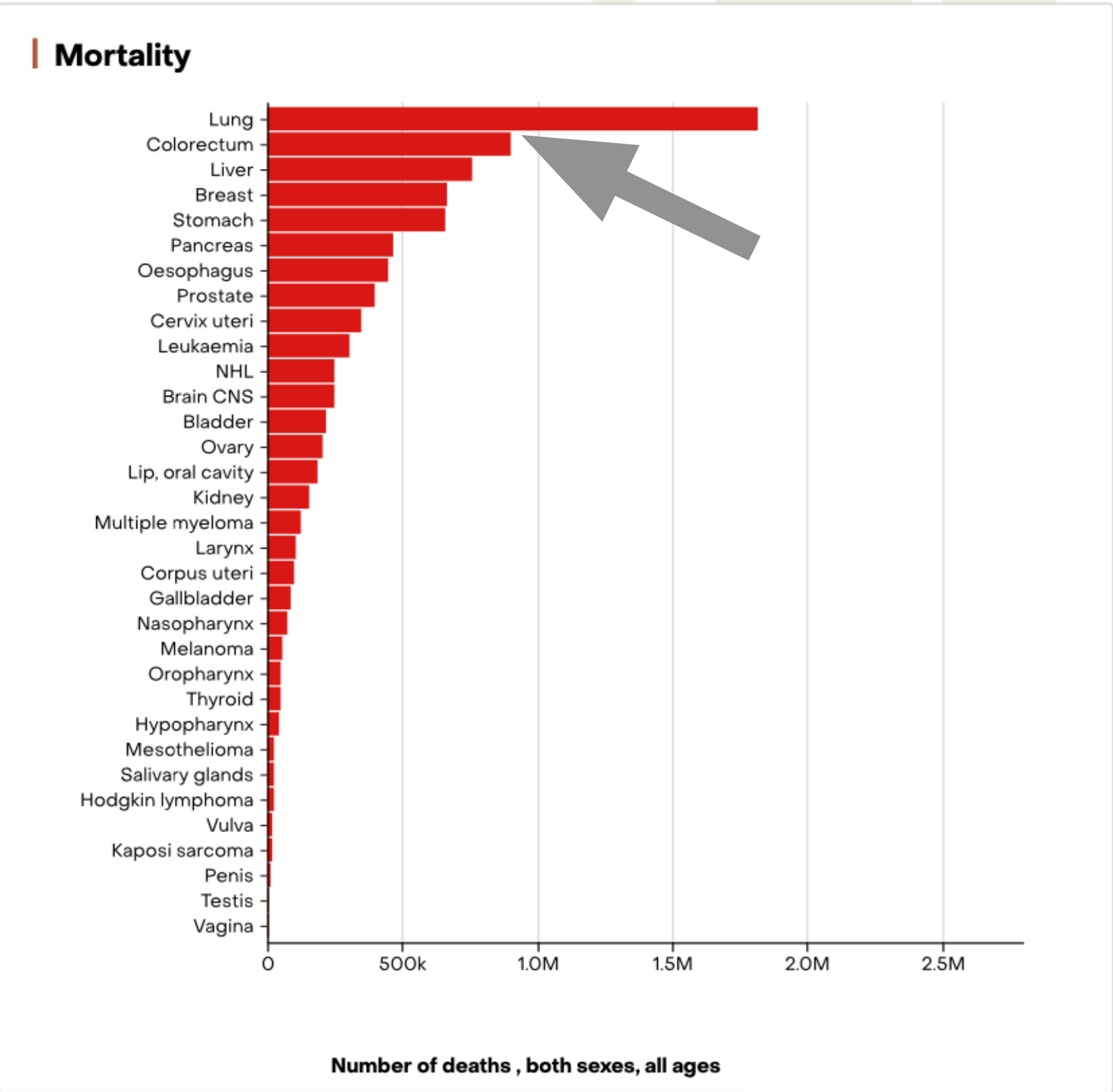
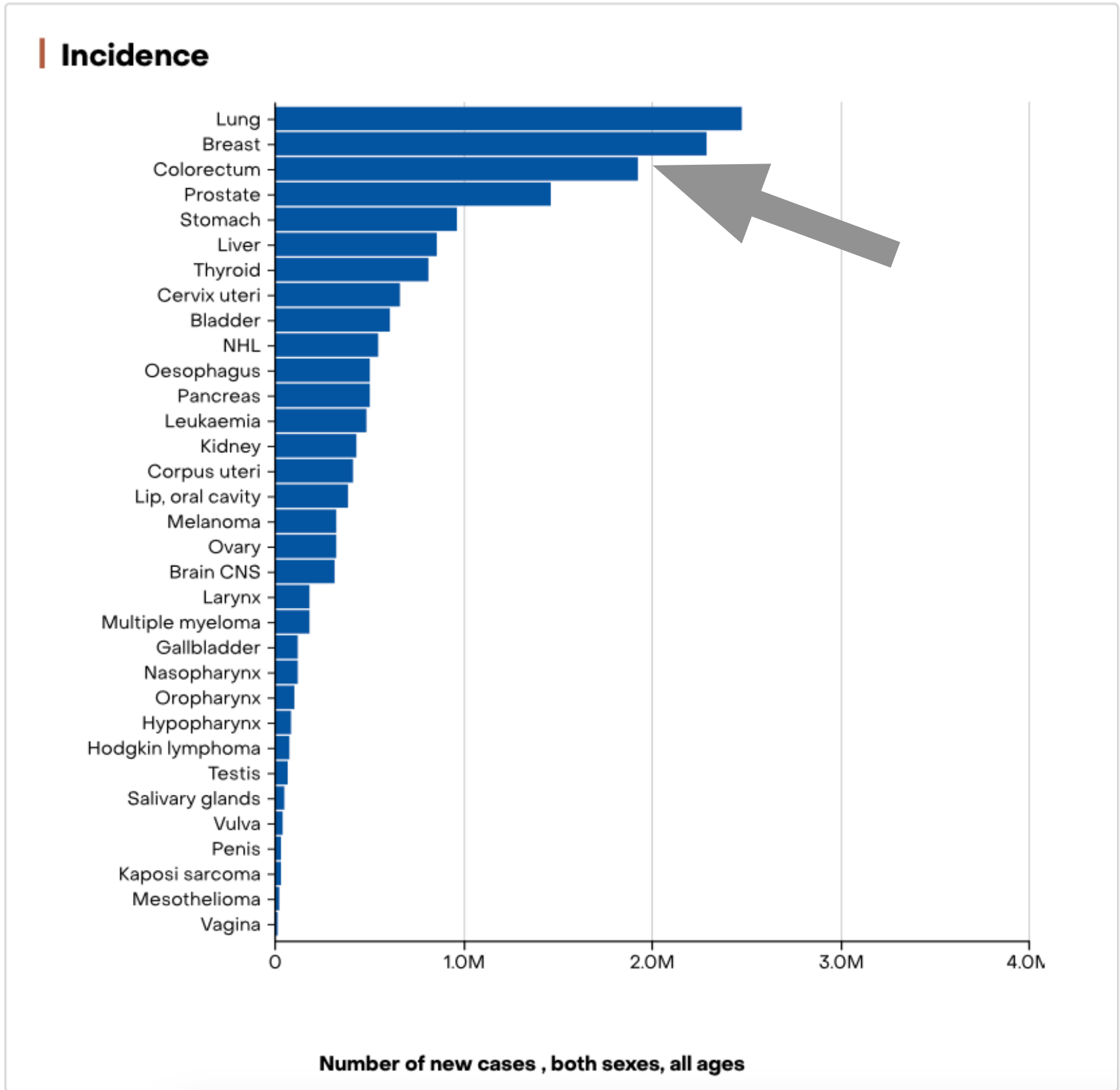
ASR (World)
196.9

Mortality

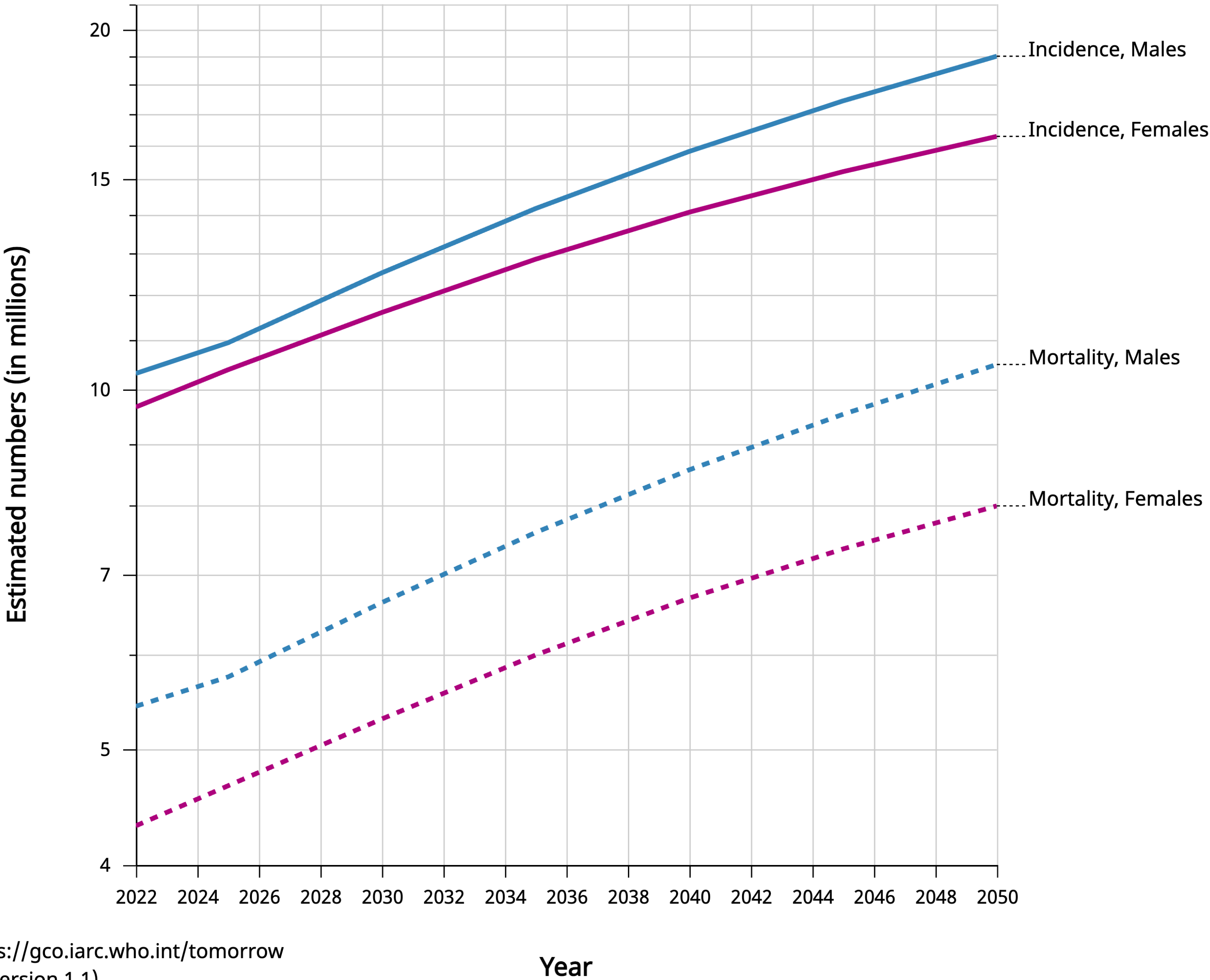
Deaths
9 743 832

ASR (World)
91.7

Cancer site ranking

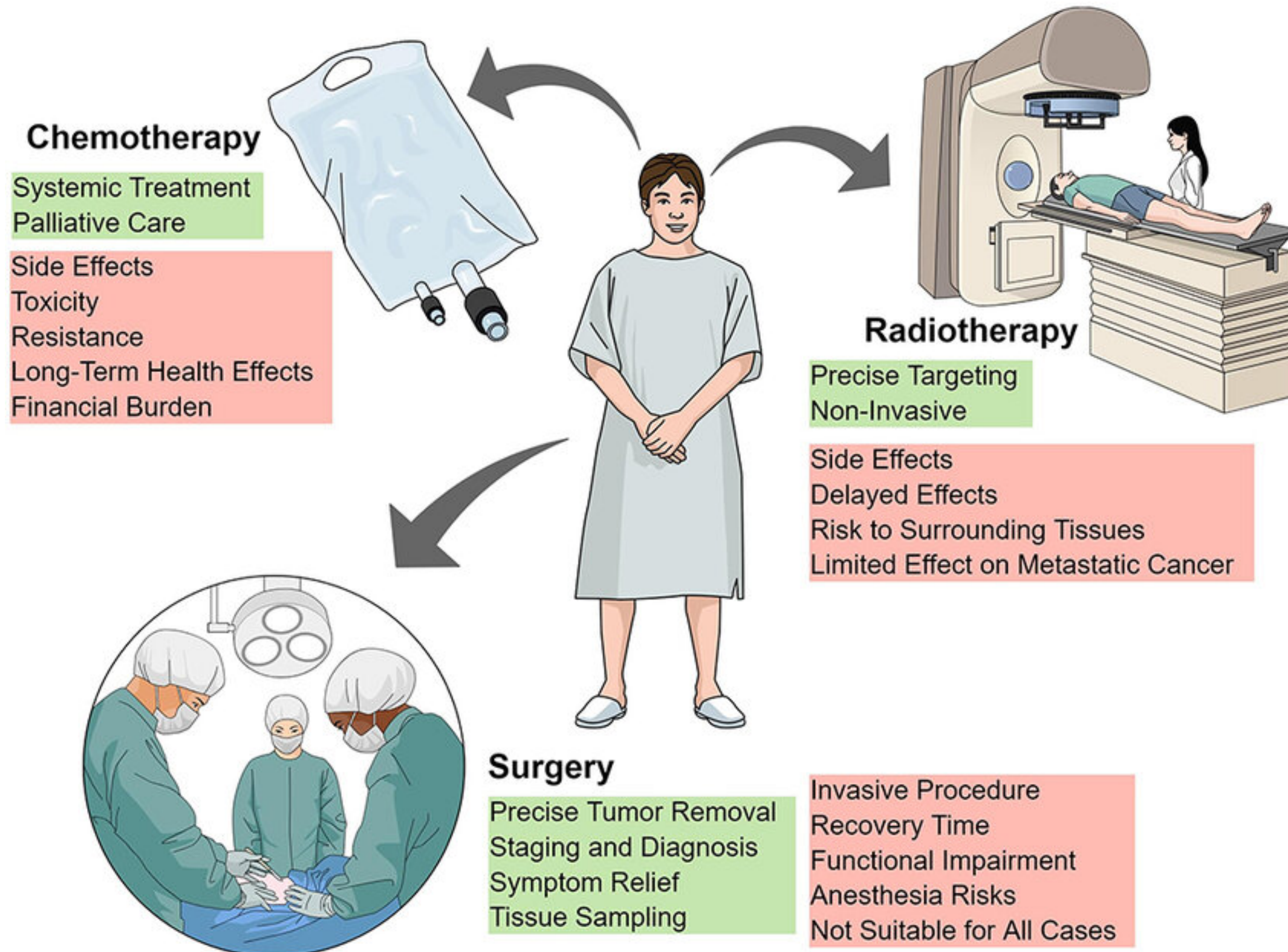


Cancer Tomorrow

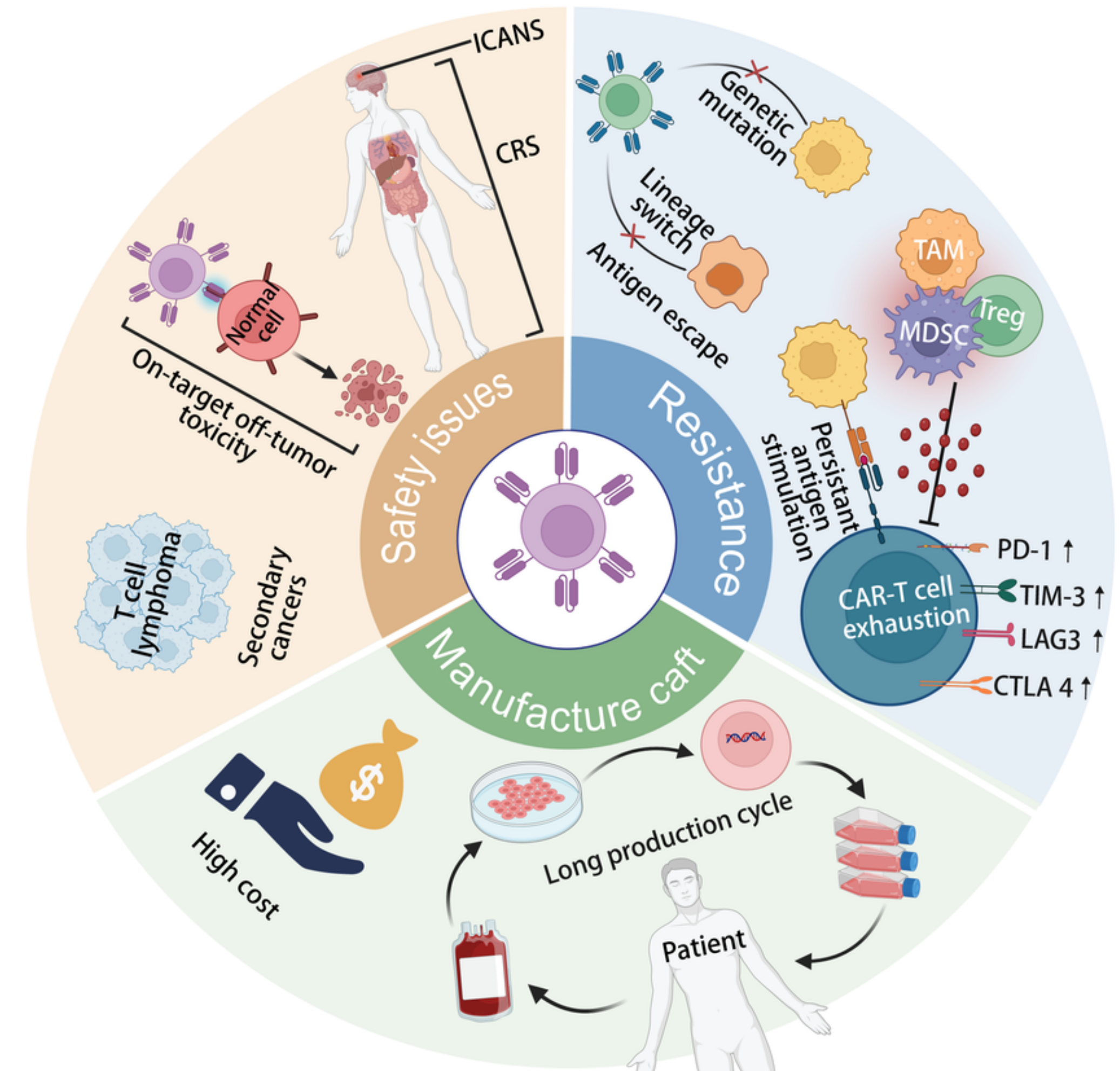


Cancer therapeutic strategies

Traditional treatments



Immune and cell therapies

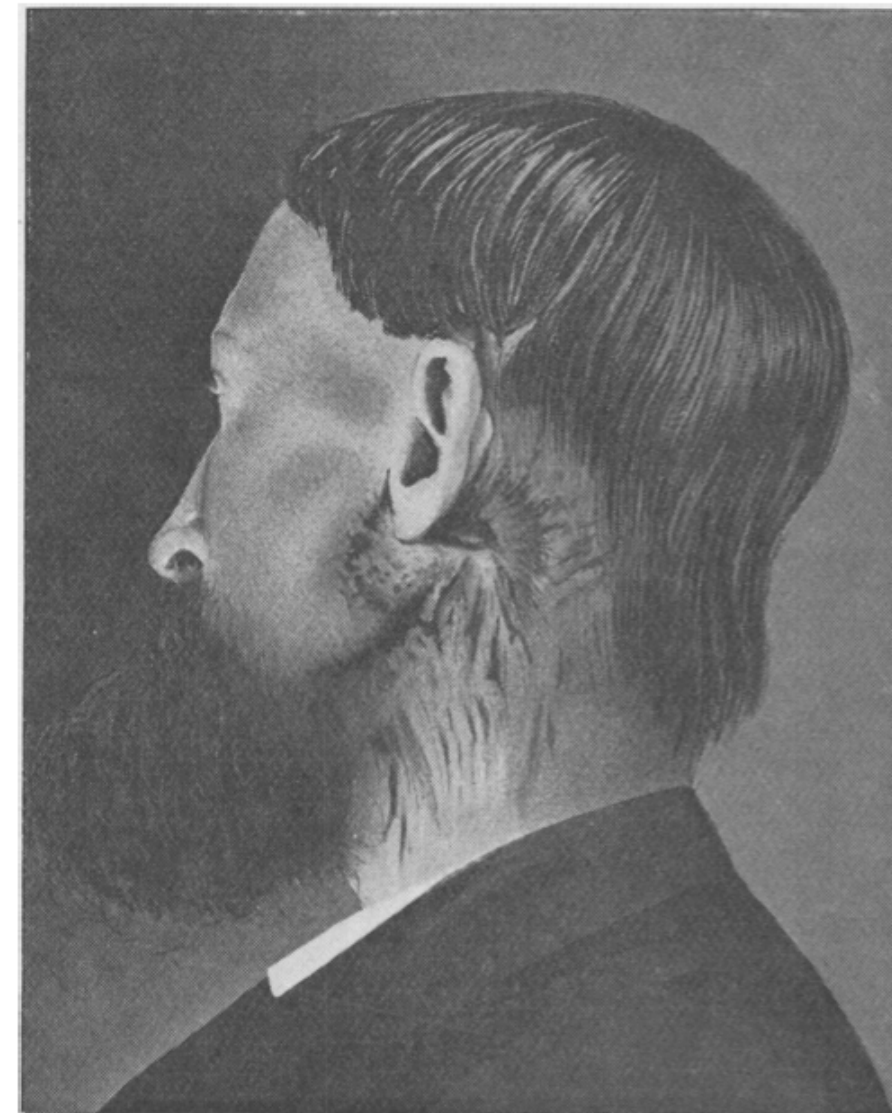


Bacterial therapeutics against cancer: more than a 100 years

1891



William
Coley

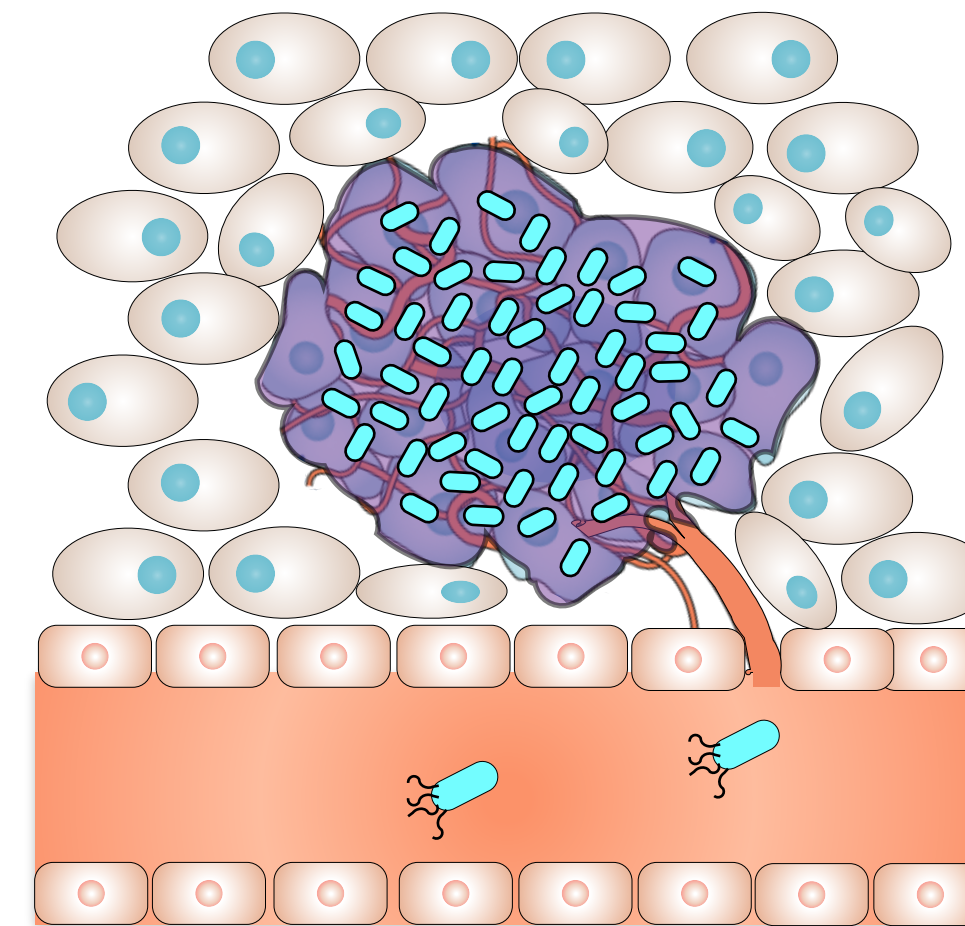


Sarcoma spontaneous regression after infection

Quelques succès mais:

- pas d'antibiotiques a cette époque
- Avènement de la radiothérapie

Hypoxie Immunosuppression



Tumor Specific colonization

Bacteria cancer therapy revival

INNOVATION

Engineering the perfect (bacterial) cancer therapy

Neil S. Forbes

Nature Review Cancer, 2010, 10 (11)

Engineered bacteria as therapeutic agents

Carlos Piñero-Lambea, David Ruano-Gallego and Luis Ángel Fernández

Current opinion in biotechnology, 2012, 35

Gene Therapy (1997) 4, 791-796
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Anaerobic bacteria as a gene delivery system that is controlled by the tumor microenvironment

MJ Lemmon¹, P van Zijl¹, ME Fox¹, ML Mauchline², AJ Giaccia¹, NP Minton² and JM Brown¹
¹Mayer Cancer Biology Research Laboratory, Department of Radiation Oncology, Stanford University School of Medicine, Stanford CA 94305, USA; and ²Centre for Applied Microbiology and

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RESEARCH

Lipid A mutant *Salmonella* with suppressed virulence and TNF α induction retain tumor-targeting in vivo

K. Brooks Low¹, Martina Itter¹, Ellen Carmichael¹, Ashok Chandra¹, Li-mou Zhen¹

***Escherichia coli* Nissle 1917 Targets and Restrains Mouse B16 Melanoma and 4T1 Breast Tumors through Expression of Azurin Protein**

Yunlei Zhang, Youming Zhang, Liqiu Xia, Xiangli Zhang, Xuezhong Ding, Fu Yan, Feng Wu
College of Life Science, Hunan Province

Bacterial Delivery of *Staphylococcus aureus* α -Hemolysin Causes Regression and Necrosis in Murine Tumors

Adam T St. Jean^{1,2}, Charles A Swofford¹, Jan T Panteli¹, Zachary J Brentzel¹ and Neil S Forbes¹
¹Department of Chemical Engineering, University of

nature medicine

LETTERS

<https://doi.org/10.1038/441591-019-0498-z>

Programmable bacteria induce durable tumor regression and systemic antitumor immunity

Sreyan Chowdhury^{1,2}, Samuel Castro¹, Courtney Coker¹, Taylor E. Hinchliffe¹, Nicholas Arpaia^{1,3,4*} and Tal Danino^{1,3,4*}

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

Engineered probiotics for local tumor delivery of checkpoint blockade nanobodies

Candice R. Gurbatri¹, Ioana Lia¹, Rosa Vincent¹, Courtney M. Treuting², Taylor E. Hinchliffe¹, Nicholas Arpaia^{1,3,4*}

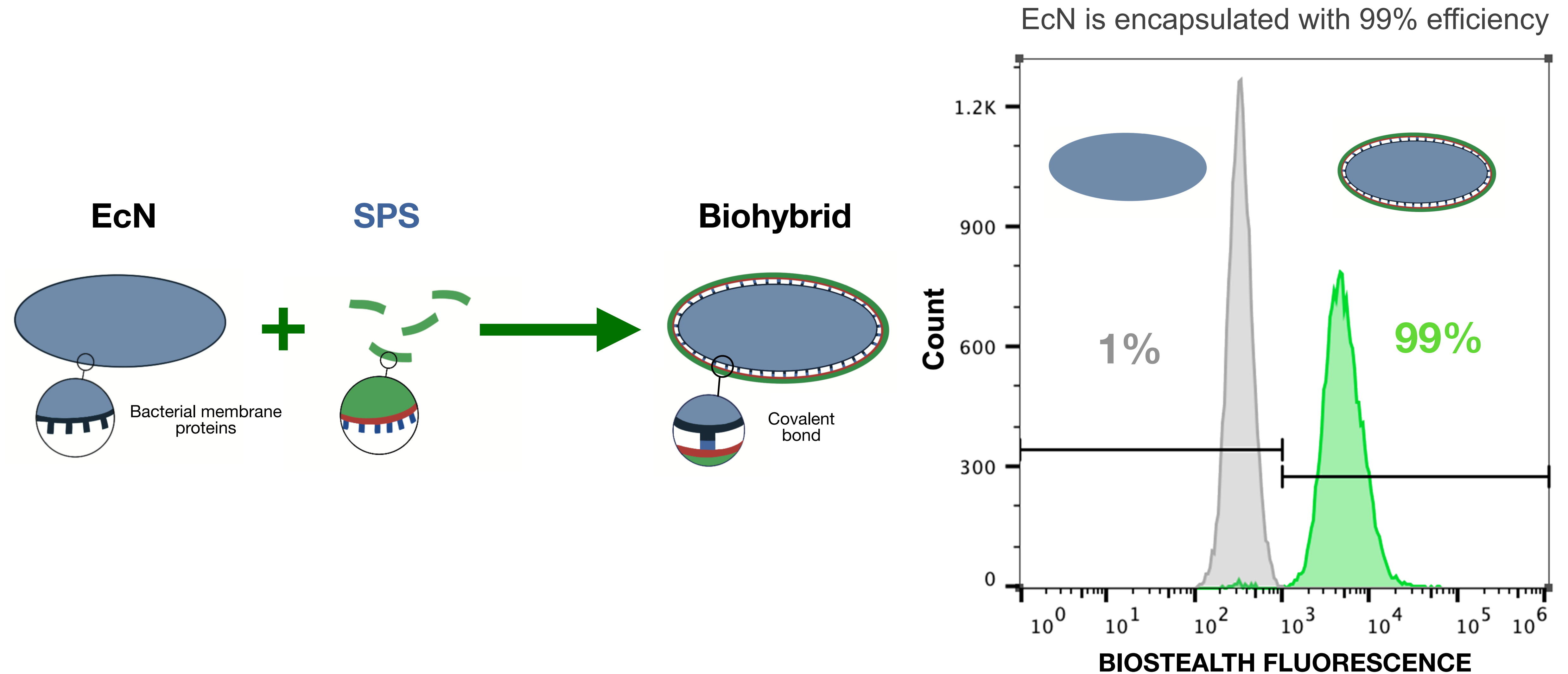
Article

Metabolic modulation of tumours with engineered bacteria for immunotherapy

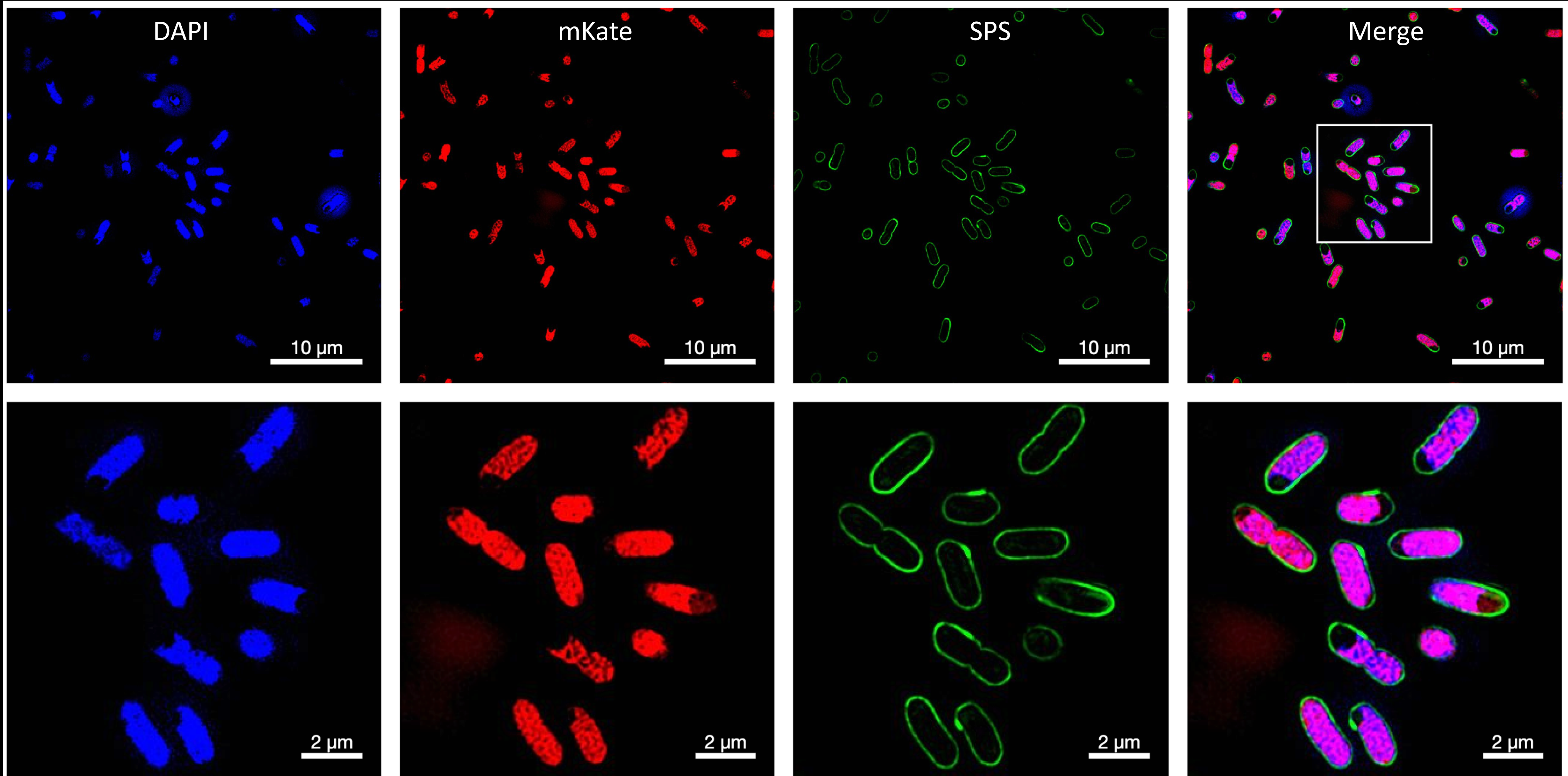
<https://doi.org/10.1038/s41596-021-04003-2> Fernando P. Canale^{1,2}, Camilla Basso^{1,3,4}, Gela Antonini¹, Michela Perotti^{1,2}, Ning Li¹, Anna Sokolovska¹, Julia Neumann¹, Michael J. James¹, Stefania Griger¹, Wenjie Jin^{1,2}, Jean-Philippe Theurillat¹, Kip A. West¹, Daniel S. Loventhal¹, Jose M. Lara^{1,3,4}, Federica Sallusto^{1,2} & Roger Geiger^{1,2,3,4}
Received: 18 May 2021
Accepted: 7 September 2021

Clinical assay show possibility to inject Billion bacteria in blood stream

iBots assembly



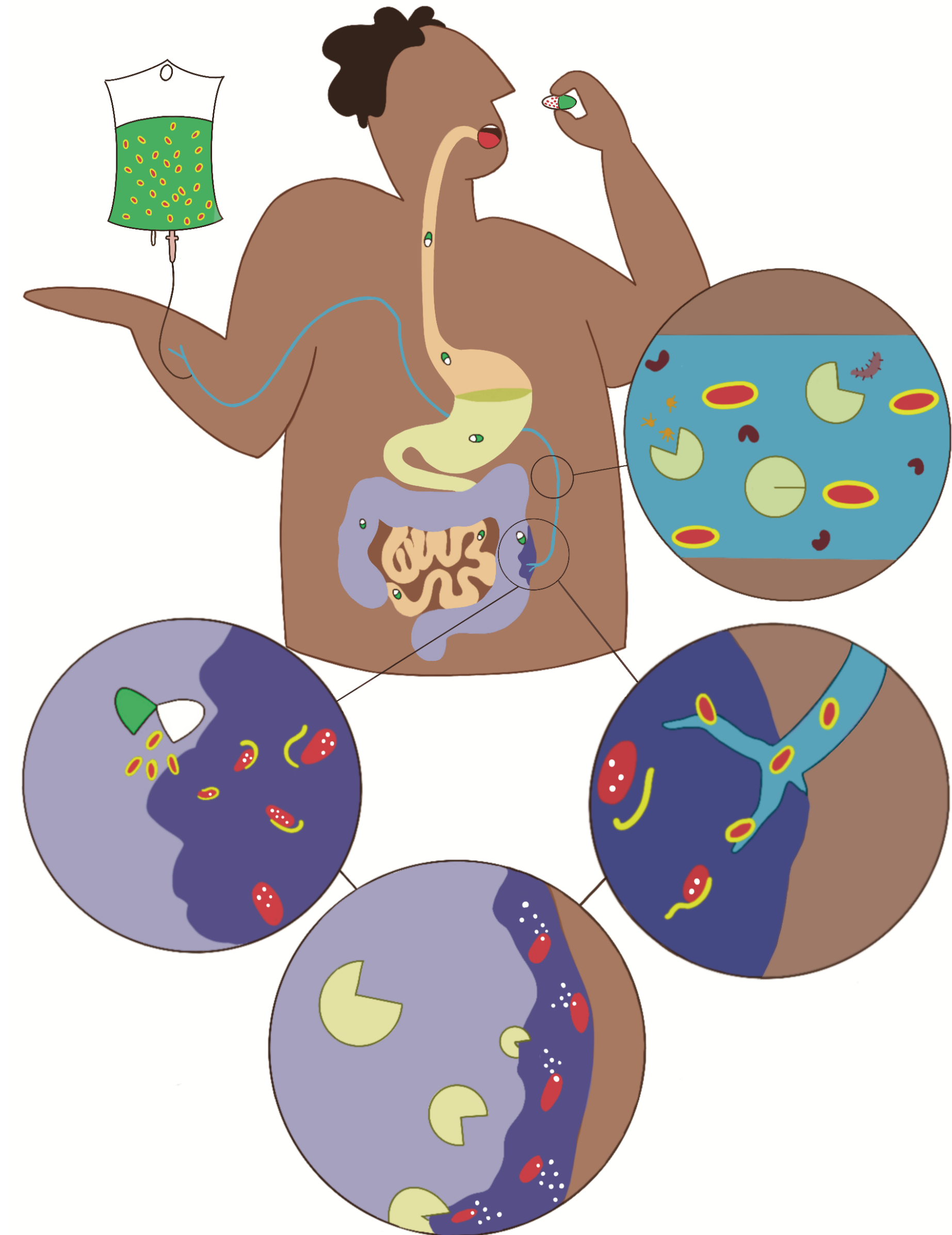
Visualization by fluorescence microscopy of EcN coated with SPS



THERABOT

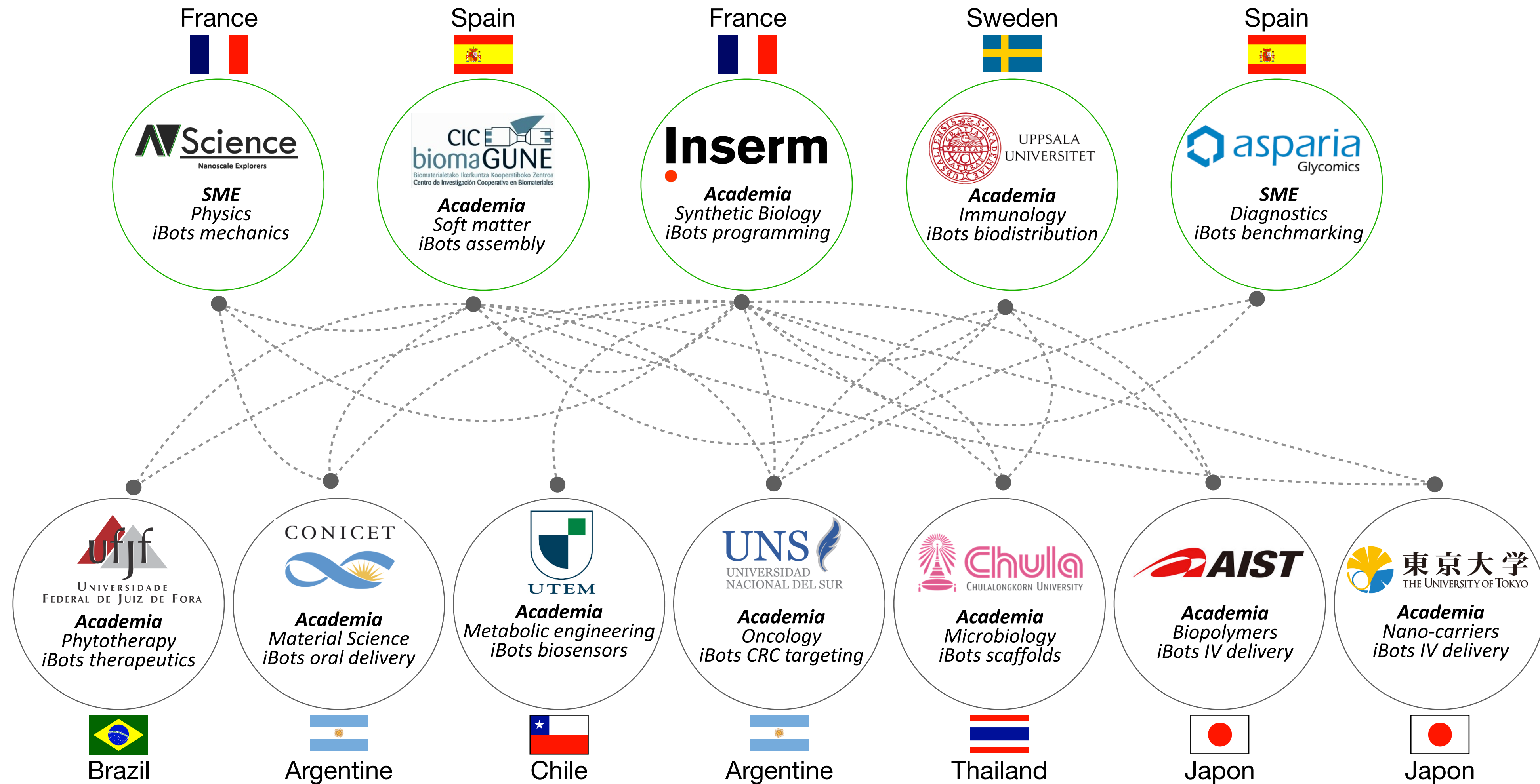
Therapeutic Bacteria Biohybrids for Oncology Treatment

GOAL: Develop an adaptable therapeutic bioagent to addresses the multifaceted challenges of cancer treatment while improving patient quality of life and reducing the cost of cellular therapies



THERABOT Consortium

European Beneficiaries



Associated partners

Our role in the project

Coordination

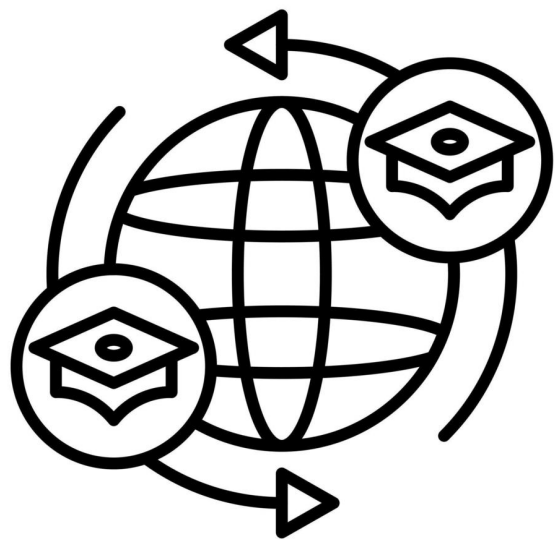
Reporting



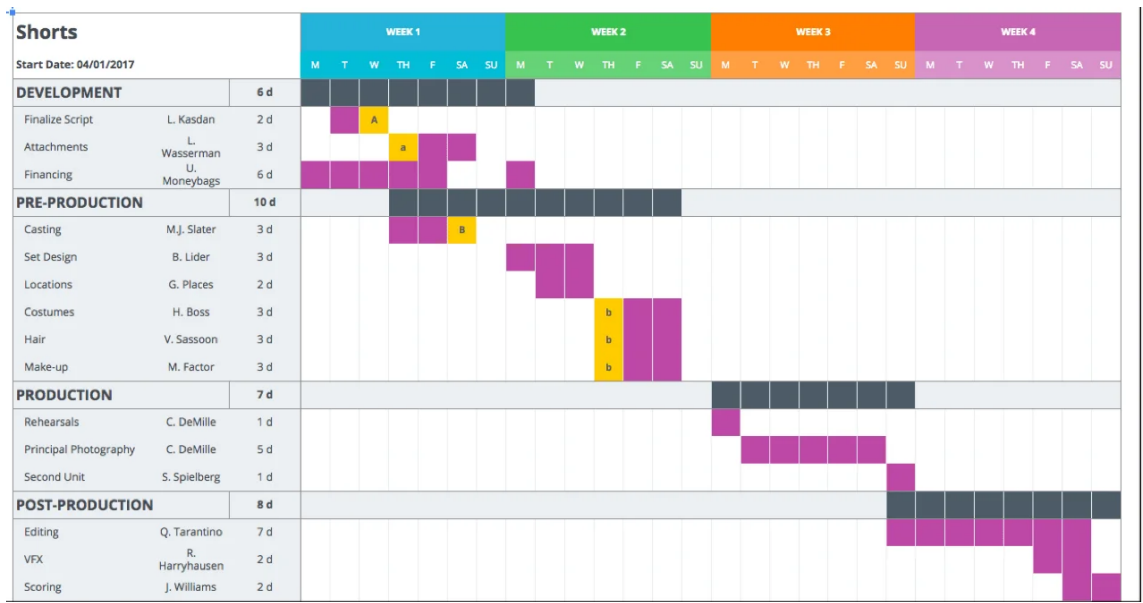
Governance



Secondments



Deliverables/Milestones



Workshops/dissemination



Bioengineering

iBots assembly



Repurposing of bacteria



Autonomous iBots



THERABOT timezones



- Pourquoi avez-vous choisi de déposer un projet européen dans le cadre de l'appel Staff Exchanges ?
- Pourquoi avoir voulu coordonner ce réseau ?
- Quels sont les retombées de ce projet (pour vous, pour les équipes, pour la recherche) ?
- Recommanderiez-vous à vos collègues de tenter l'aventure ?
- Quels conseils et points d'attention pourriez-vous leur donner ?

THANK YOU FOR YOUR ATTENTION