

N E W L A Y O U T

1,000,000,000 CHF investment

7,000,874 hours of work

6,587 experiments

423 researchers

1 medicine



With Prof Susan M Gasser
and Prof Olivier Michielin

THE MAKING OF AN INNOVATIVE MEDICINE

*Introductory workshops on translational biomedical research and drug discovery
and development*

**BIO-698 resumes Thursday September 21. 2023
4:15 PM @ AAC 108**



Sciences de la Vie -SV



Prof Roger G. Clerc

The Making Of An Innovative Medicine – course schedule

Thursday's @ 4-6 PM except 14.12/21.12.23 @2-6 PM



Session 1: Scope of the **course _ general organization _** case study

21.09.23 *Embracing a career at the heart of biomedical research !?*

AAC108

Session 2: **Historical perspective:** the modern pharmacy

28.09.23 *Advent of modern medicines - placebo controlled drug development*

AAC108

Session 3: Introduction to **translational research:** crossing the bridge

05.10.23 *A chasm has opened wide between biomedical research and patients in need*

AAC014

Session 4: **Therapeutic target identification I & II**

12-19.10.23 *"me too" vs a wealth of innovative targets _ small MW cpds vs biologicals*

AA014 AAC108

Early front loading of biomarker identification for cohort stratification

Session 5: Structure based drug design _ medicinal chemistry _ low/high throughput

26.10.23 screening assays _ multiple parallel parameters optimization MDO

AAC108

Setting up screening assays, the robotics, the million cpds libraries

Session 6: Therapeutic modalities **peptides and biologicals:** today's -

02.11.23 tomorrow's pharmacy NBEs

AAC108

Challenges (cost of goods - healthcare payers) and opportunities

WORKSHOP LISTING - THE MAKING OF AN INNOVATIVE MEDICINE BIO698

! NON EXHAUSTIVE LISTING - SUGGESTIONS WELCOME !

sessions	no	workshops	speaker/s
S02 (28-09-23) ! AAC108 !			
historical medicines	1	vaccine discovery : E. Jenner and smallpox	Danica M
with Nobel laureates while	2	penicillin: impact, whose invention ?	
hopping on giant shoulders	3	prozac at the core of psychiatry	
	4	lipitor/statins at last a blockbuster	
	5	artemisinin and malaria	Umair
	6	cyclosporin from soil sample to blockbuster	Umair
S03 (5-10-23) ! AAC014 !			
translational research	7	expanding the scope of targeted therapies	
an emerging field	8	chronotherapy	Pitt
S04 (12-10-23) ! AAC014 !			
therapeutic target identification	9	rare diseases repurposing medicines	Adrien
S04b (19-10-23) ! AAC108 !	10	nocosomial inf/MRSA/phage antibacterials	Georges
therapeutic target identification	11	Crispr/Cas9 gene editing huntington disease	Pitt
	12	AI in drug discovery	Simon
S05 (26-10-23) ! AAC108 !			
structure based drug design	13	macrocycles and non druggable targets	Masota
	14	chemoproteomics - NMEs	Nico G
S06 (02-11-23) ! AAC108 !			
therapeutic modalities - NBEs	15	Biologicals/biotech production/Incretins	Tim F
	16	armed monoclonal AB medicines	Nico G
	16	RNA therapeutics, antisense medicines	
S07 (9-11-23) ! AAC108 !			
PHC personalized healthcare	17	BRCA1 preventive surgery/tumor board	Nikita
Human genomics	18	SOPHIA Genetics - GWAS	
	19	disease enabling biomarkers/micro RNAs	Isika
S08 (16-11-23) ! AAC014 !			
pharmacogenetic polymorphism	20	NextGenSequencing - precision medicine	Hien
	21	deCODE Inc pharmgenomic/iceland genealogy	
S09 (23-11-23) ! AAC108 !			
in vivo pharmacology	22	organoids come of age	Nathalie B
toxicology	23	thalidomide repurposing	Ekaterina
S10 (30-11-23) ! AAC108 !			
clinical research	24	AI medicine 2.0	Simon
	25	most common genetic defect : cystic fibrosis	.
	26	sex bias in preclinical and clinical research	Weilin
	27	placebo/nocibo effects	Tim ?
S11 (07-12-23) ! AAC108 !			
intellectual property/integrity	28	SMA gene therapy - pay for performance	Abtin
	29	biopatents - 23 and Me - my genome	khosiyat
S12 (14-12-23) starts @ 2PM		Hacking medicine	all + invitees
! MED21522!			
S13 (21-12-23) start @ 2 PM		Hacking medicine	all + invitees
! AAC231 !			



Workshops _ The Making Of An Innovative Medicine (non exhaustive listing)



- Introduction to biomedical translational research : crossing the bridge
- What do you think is translational research all about ?





- An **emerging biomedical research concept** that brings together 2 distinct groups of researchers together towards a common goal: a quantum jump in advancing healthcare and drug discovery for patients in need





TRANSLATIONAL RESEARCH

**The Application of the
Scientific Method to
Address a Health Need**

Translational research : do what patients need next !



FROM BENCH TO BEDSIDE AND BACK !

Basic research :
the scientific
method

Clinical research :
the health need



The goal is to
learning
communicating
across disciplines to
achieve advances in
health care.



WHY ?
HOW ?



- PhDs, MD-PhDs WITH TREMENDOUS EXPERIENCE IN QUANTITATIVE MOLECULAR BIOLOGY AND MOLECULAR PATHOLOGY, UNRAVEL UNDERLYING MOA OF DISEASE



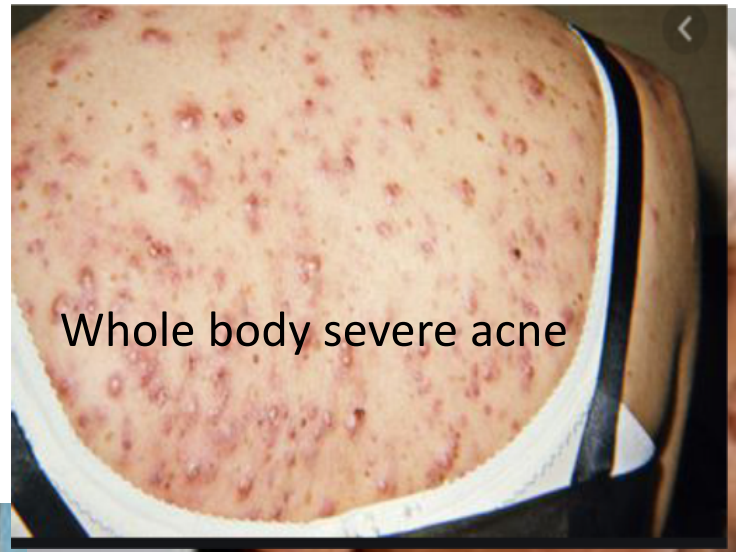
- CLINICIANS MDs NURSES WITH EXTENDED EXPERIENCE IN CLINICAL RESEARCH AND PATIENT IN NEED

High unmet medical needs : do now what patients need next !



**oncology patient in need
evasive resistance in cancer**

**neurodegenerative ailments
psychosomatic stress
autism alzheimer schizophrenia**



Whole body severe acne



chronic migraine



rheumatoid arthritis patient

**multiresistant bacterial
infections and multiple
pathophysiological
consequences**



**WHICH MEDICINE CAN HELP
ME ? WHICH PROTEIN
PERTURBATION CAN HELP ME ?
IS THERE A SOLUTION ?**



MI CVD, T2D etc

Is your research project translational ?



**Translational Research
Differs from Scientific
Discovery Research in its
Goal and Methods**

Translational research combines health and underlying disease knowledge



Comparison of Scientific Discovery and Translational Research

Scientific Discovery

Translational Research

Scientific Opportunity

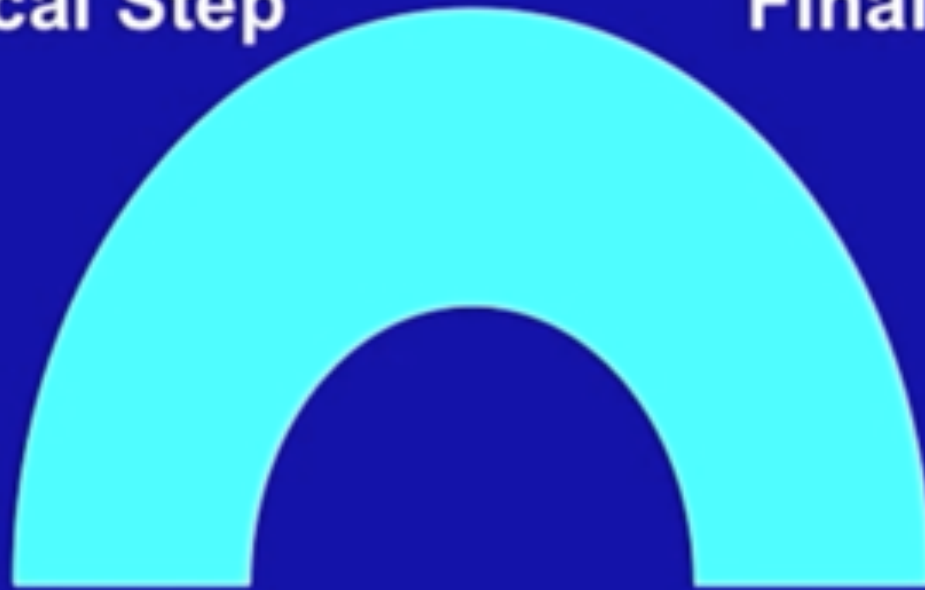
Health Need

Next Logical Step

Final goal

Knowledge

Health





The 3 Dimensions of Clinical and Translational Research

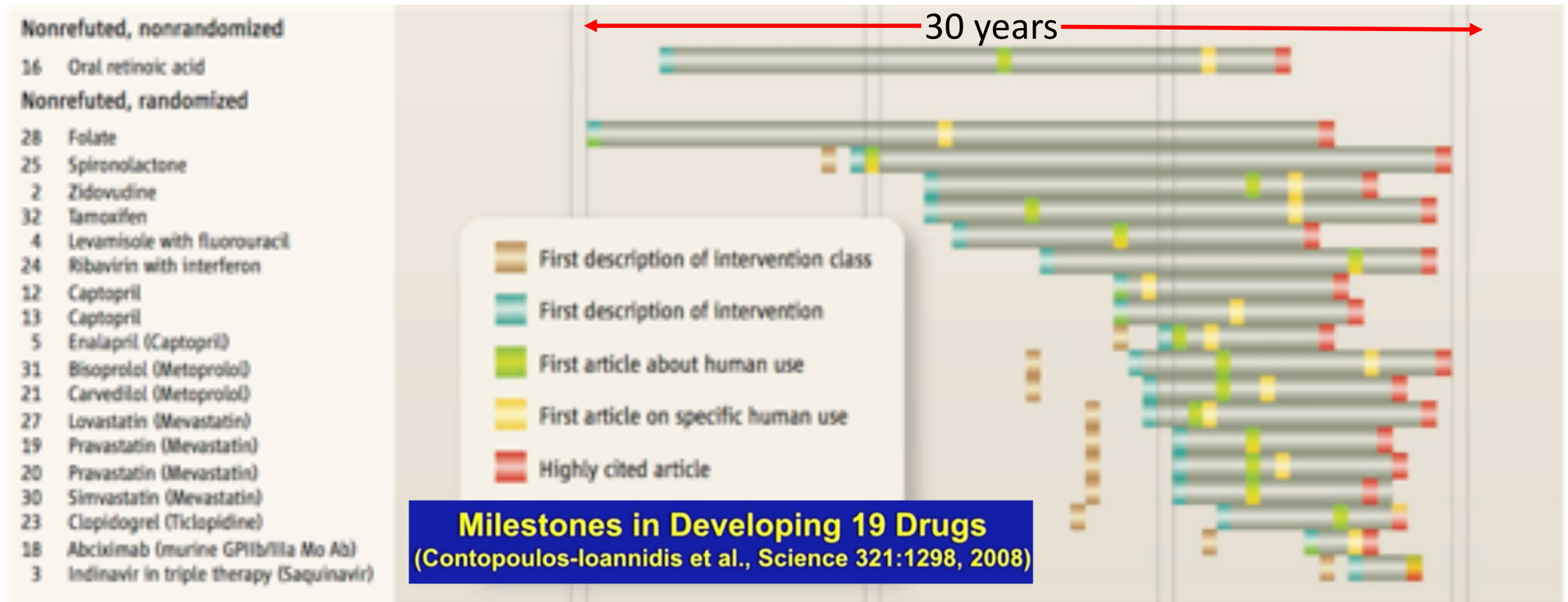
- **Multidisciplinary team building**
- **Integration across the entire T1 to T2 spectrum**
- **Integration of academic discipline with governmental agencies (granting, public health, regulatory), industry, philanthropy, and patient advocacy groups**



The Essentials Skills of the Translational Research Investigator or Team

**3. The ability to conceptually
design a Phase 3 study to assess
safety and efficacy before
embarking on the project**

Increasing time lag between DISCOVERY AND TRANSLATION: Are you going to wait for decades to get a cure to your ailment ?



- Among 18 non refuted interventions in randomized trials the translation lag was 16.5-22 years
(the fastest successful translation occurred for eg. indinavir (Crixivan HIV patients) which took 4 years and Dornase (Pulmozyme CF patients) 5 years)



Translational research is facing the road block of ancient research programs

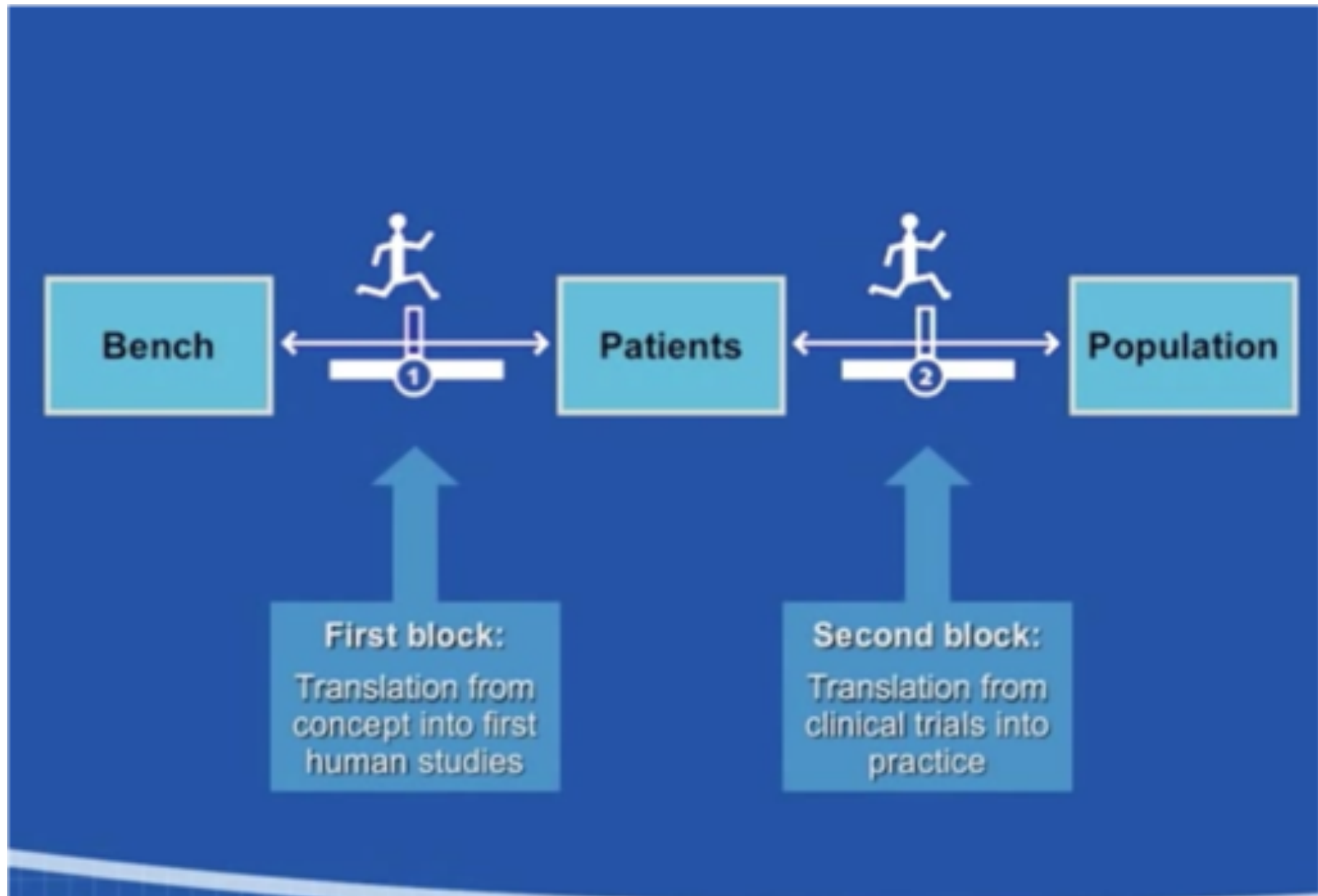


A Translational Block..... Back to 19th century medicine ?



- *Mainstream biomedical research : mutual supports between patients and research scientists : take advantage eg. of **patient derived iPSC** for the identification of novel medicines – therapeutic targets*
- *Shuttling solid/liquid biopsies and biomarkers from bench to bedside and back allow monitoring the efficacy and safety of a medicine in real time*

Translational research_ major road blocks



Healthcare research : complexity increases : crossing the valley of death ?



A chasm has recently opened up
between biomedical researchers and
the patients in need – the pitfalls

Basic research $\longleftrightarrow$ Clinical research



Cartoonist Nature News and Views 2018

- costs of developing a new medicine mounts today at >1000.000.000 US \$!
 - attrition rate !
 - healthcare providers closed to bankruptcy (failure rate 99% : who wants to invest in this ?)

and healthcare costs exploding : people are tired of paying insurances

- life expectancy scaling up or down ?

**“CROSSING THE VALLEY OF DEATH” ?...
DO NOW WHAT PATIENTS NEED NEXT !**

- eg. pharmacogenomics allows the stratification of cohorts (eg. deCODE Inc) : who owns your DNA ?
- personalized medicine/precision medicine : solution or next problem?

Lausanne - Switzerland – 2018 - a new center for translational biomedical research in ONCO IMMUNOLOGY is born : AGORA



Agora Translational Oncology Res

BREAKING NEWS



KEY CONCEPT : BRINGING TOGETHER BIOMEDICAL SCIENTISTS AND CLINICIANS WHO DO NOT NORMALLY INTERACT WITH ! WIDE OPEN DOORS TO « PERSONALIZED HEALTHCARE » !

Lausanne _ Switzerland _ a new center for translational
biomedical research in ONCO IMMUNOLOGY is born : AGORA

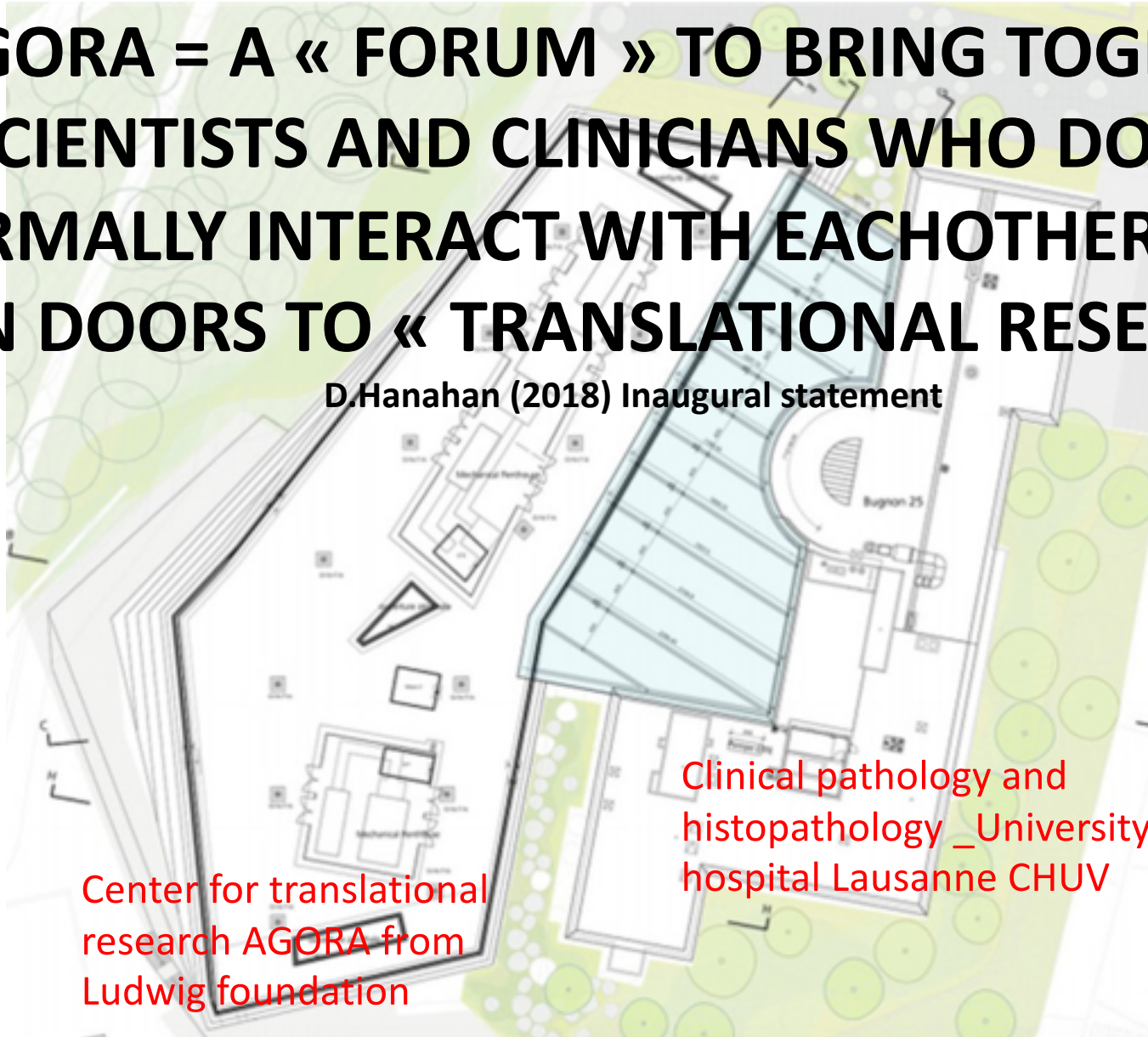


**AGORA = A « FORUM » TO BRING TOGETHER
SCIENTISTS AND CLINICIANS WHO DO NOT
NORMALLY INTERACT WITH EACH OTHER ! WIDE
OPEN DOORS TO « TRANSLATIONAL RESEARCH » !**

D.Hanahan (2018) Inaugural statement

Center for translational
research AGORA from
Ludwig foundation

Clinical pathology and
histopathology _ University
hospital Lausanne CHUV



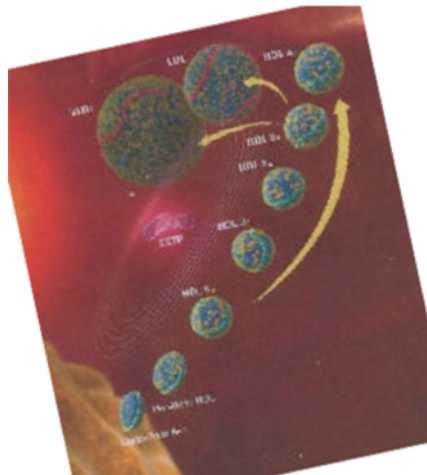
TRANSLATIONAL RESEARCH : a forum for clinical and exploratory research scientists to meet and discuss



Basic research ↔ Clinical research



DO NOW WHAT PATIENTS NEED NEXT !



UNIVERSITÄT BASEL

PharmaCenter



Basel Translational Medicine Seminar

A Forum for Clinical and Basic Scientists to Meet and Discuss

High Density Lipoproteins, Dyslipidemia and Coronary Heart Disease

Welcome, Introduction and Moderation

Prof. Dr. Roger G. Clerc, Hoffmann-LaRoche, Basel, Switzerland

Shaping HDL Functionality with CETP: a new look at the HDL/CETP controversy

Dr. Eric J. Niesor, Hoffmann-LaRoche, Basel, Switzerland

CETP Inhibition and Cardiovascular Prevention

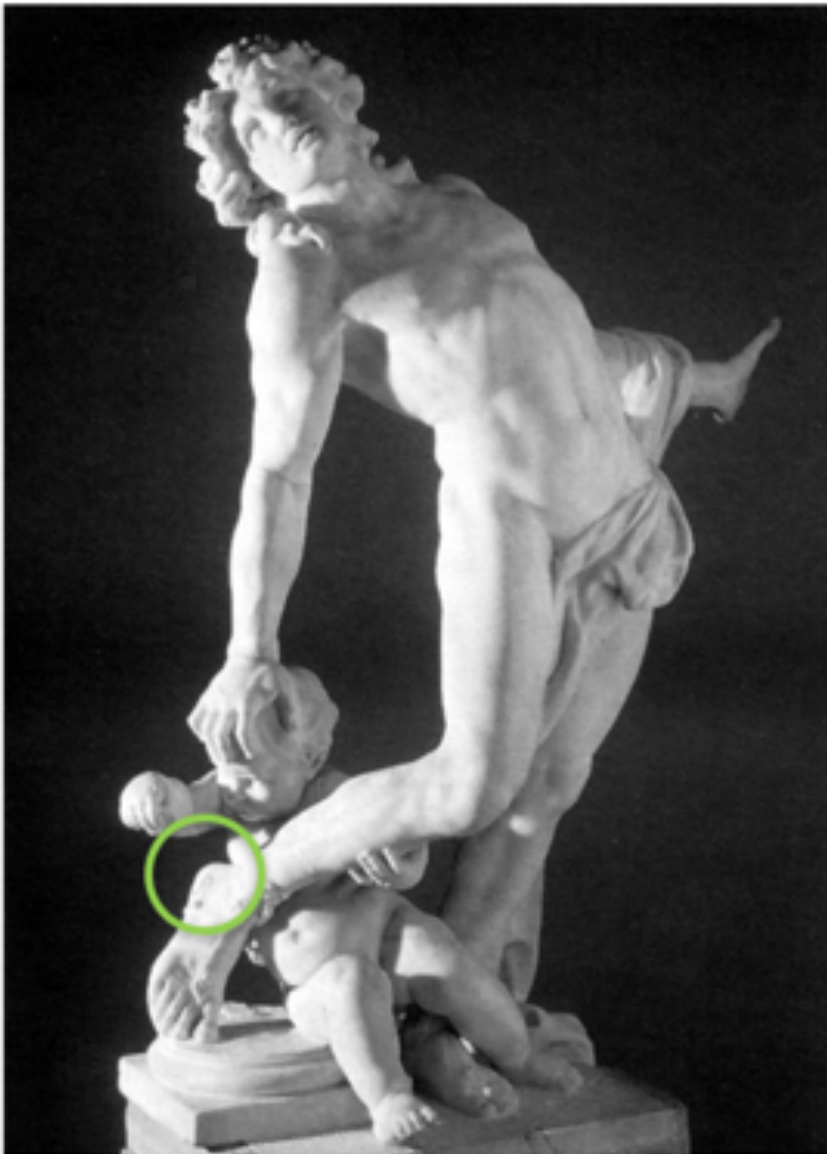
Prof. Dr. Thomas F. Lüscher, Chairman of Cardiology, Cardiovascular Center, University Hospital Zürich, Switzerland

Round Table Discussion with expert panelists

Thursday, Sept 22, 2011, 18:00-19:30, Pharmazentrum Lecture Hall 1



Cancer → > 250 devastating diseases



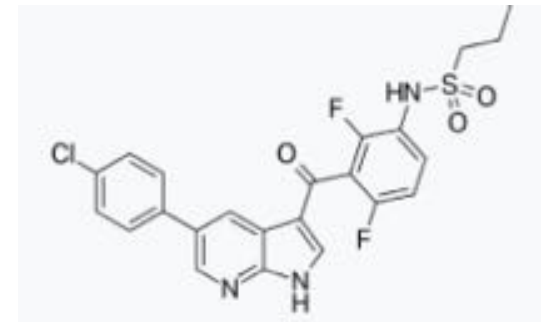
We dream of

- **Achilles' heels**
« THE vulnerable spot »
- **Magic bullets**
« THE innovative target »
- **Miracle Drugs**
« THE precision medicine »

Translational research : evasive cancer drug resistance to targeted therapies : a recurrent theme



Clinical efficacy of Vemurafenib



B-RAF kinase inhibitor Vemurafenib

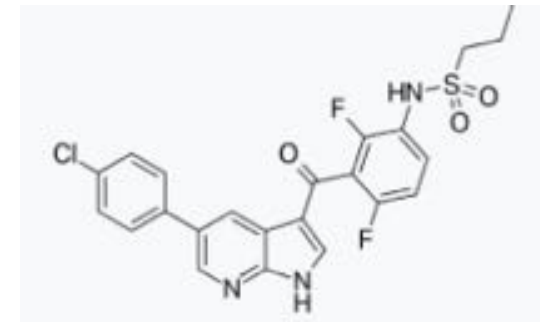
- Vemurafenib interrupts the B-Raf/MEK step in ErK pathway if B-RAF has V600E mutations (BRAF inhibitor)
- Target the BRAF V600E mutation (FDA approved in 2011)
- Metastatic melanoma (most common mutation V600E)
- Aggressive form of skin cancer
- Programmed cell death in melanoma cell lines
- **EVASIVE CANCER DRUG RESISTANCE !**



Translational research : evasive cancer drug resistance to targeted therapies : a recurrent theme



Clinical efficacy of Vemurafenib

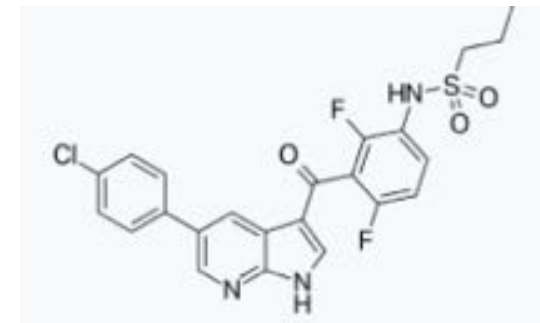


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B-RAF kinase inhibitor Vemurafenib

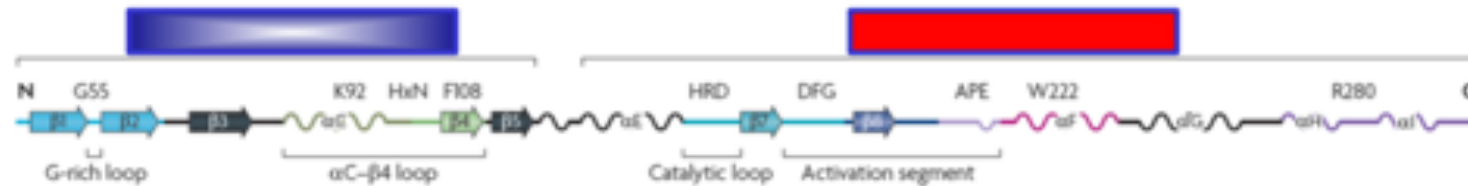
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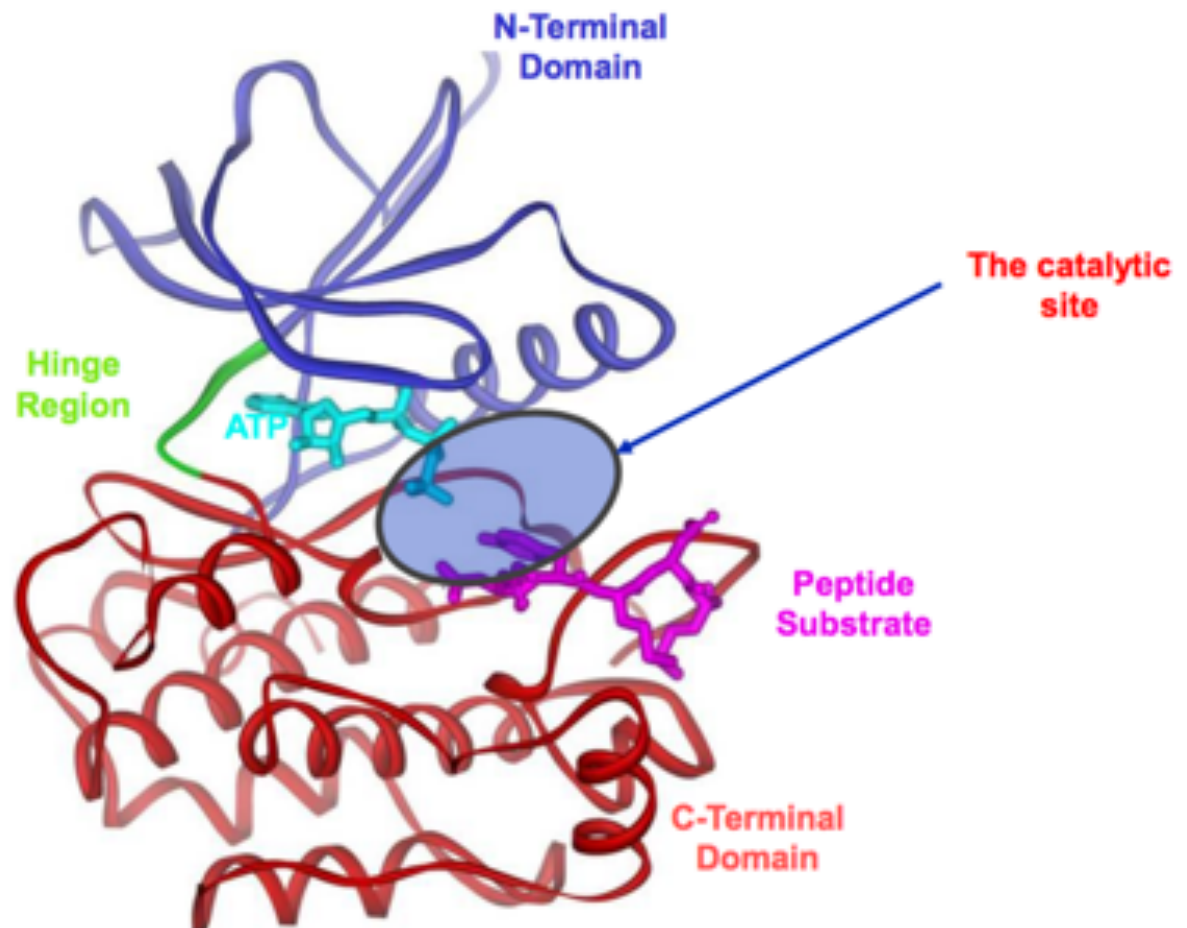
Most cancer medicines are targeting protein kinases a prototype of a druggable therapeutic target



Kinase Domain = Catalytic Site



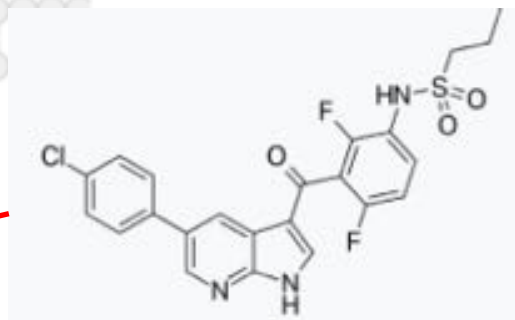
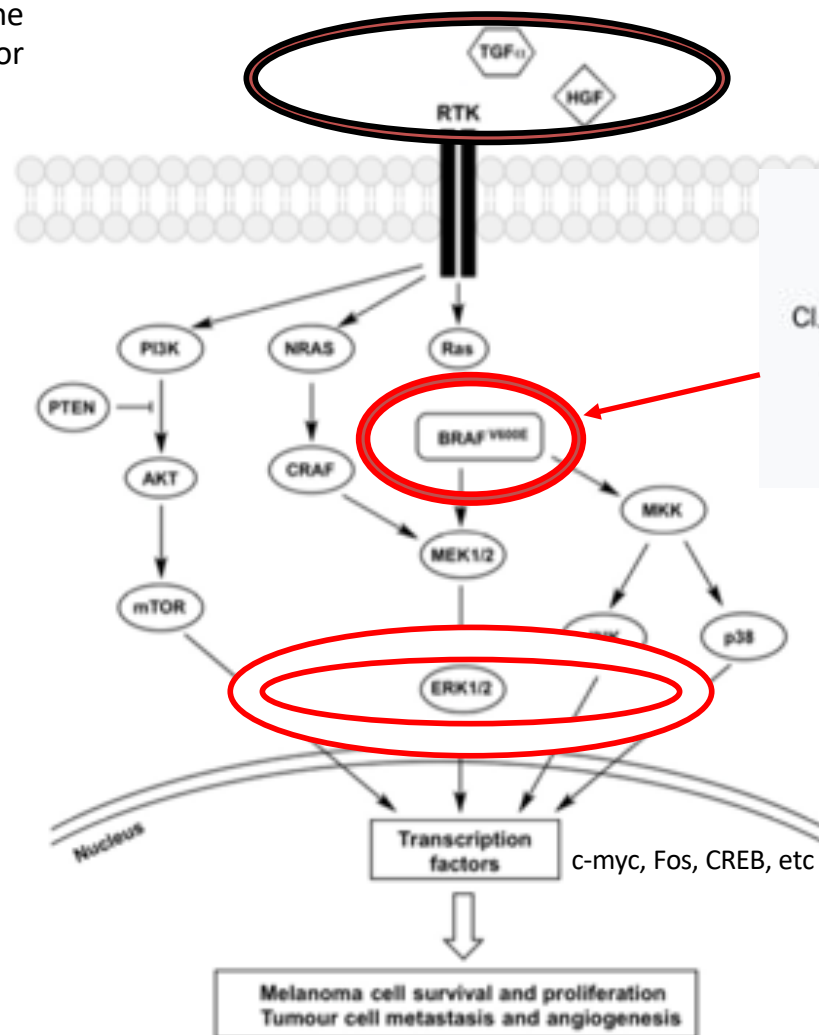
What about
kinase allosteric
modulators ?



Translational Research: evasive cancer drug resistance : a recurrent theme with melanoma patients



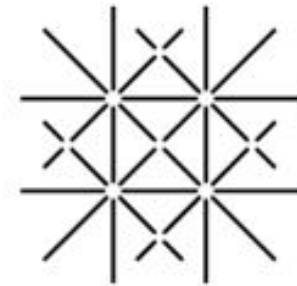
TGF- α plays a role in the processes involved with tumor initiation and tumor growth.



BRAF mutations have been described affecting BRAF gene: gene copy number gain or amplification of BRAF, and alternative splicing of BRAF resulting in overexpression and leading to reactivation of ERK independently of RAS

Figure 1. Mechanisms of BRAFi resistance converge on constitutive ERK signalling. Regardless of its upstream activator RAS, BRAF^{V600E} is constantly activated, and vemurafenib treatment was shown to inhibit the kinase. However, the increased secretion of growth factors (HGF and TGF- α) coupled with the overexpression of receptors (PDGFR β , IGFR1, EGFR and c-Met) trigger the activation of signalling

TRANSLATIONAL RESEARCH IN ACTION: quantitative phosphoproteomics allows to trace evasive cancer drug resistance

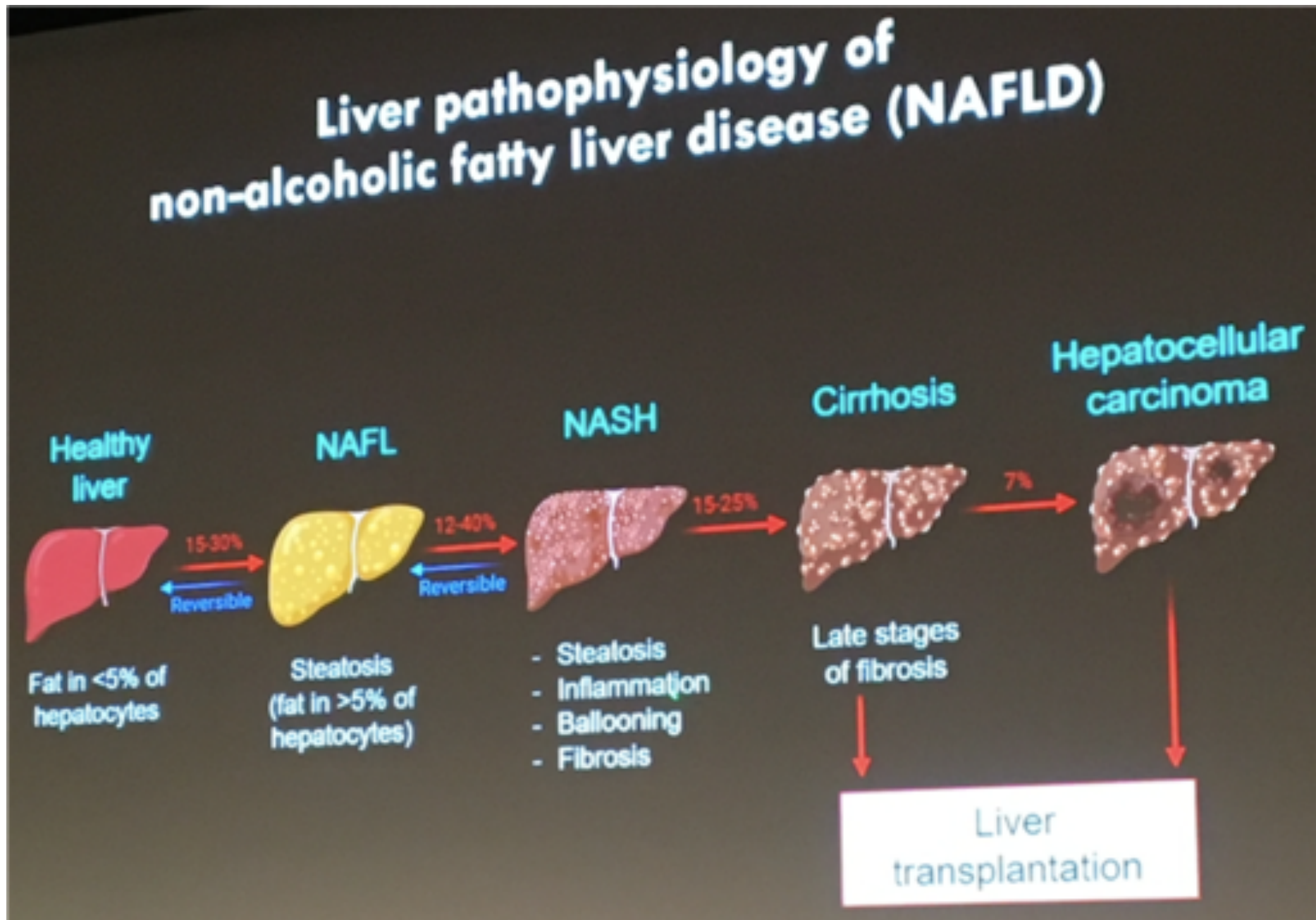


UNI
BASEL

BIOZENTRUM

Universität Basel
The Center for
Molecular Life Sciences





Translational Research: longitudinal studies allows
to trace in patients evasive cancer drug resistance



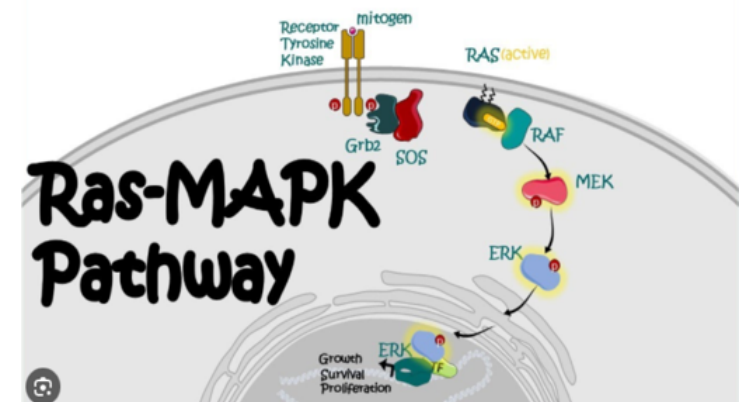
1. HOW DOES THE ACTIVITY OF CANCER SIGNALING PATHWAY CHANGE DURING THERAPY ?

Quantitative proteomics and phosphoproteomics on
serial tumor biopsies from a sorafenib-treated
HCC patient

Eva Dazert^a, Marco Colombi^a, Tujana Boldanova^b, Suzette Moes^a, David Adametz^c, Luca Quagliata^d, Volker Roth^c,
Luigi Terracciano^d, Markus H. Heim^b, Paul Jenoe^a, and Michael N. Hall^{a,1}

^aBiozentrum, University of Basel, 4056 Basel, Switzerland; ^bDepartment of Biomedicine, University Hospital Basel, 4031 Basel, Switzerland; ^cDepartment of
Mathematics and Computer Science, University of Basel, 4051 Basel, Switzerland; and ^dMolecular Pathology, University Hospital Basel, 4003 Basel, Switzerland

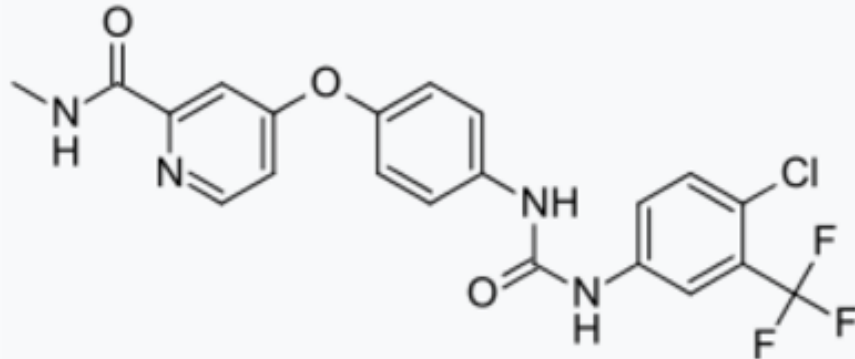
2. CAN CHANGES IN PROTEINS p-SITES BE LINKED TO TUMOR PROGRESSION OR RESISTANCE ?



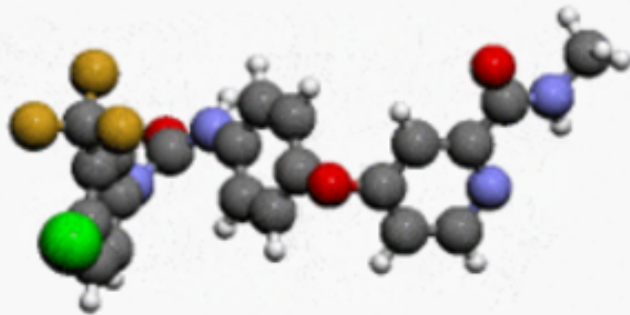
Multikinase inhibitor sorafenib as exemplary pioneer experiment



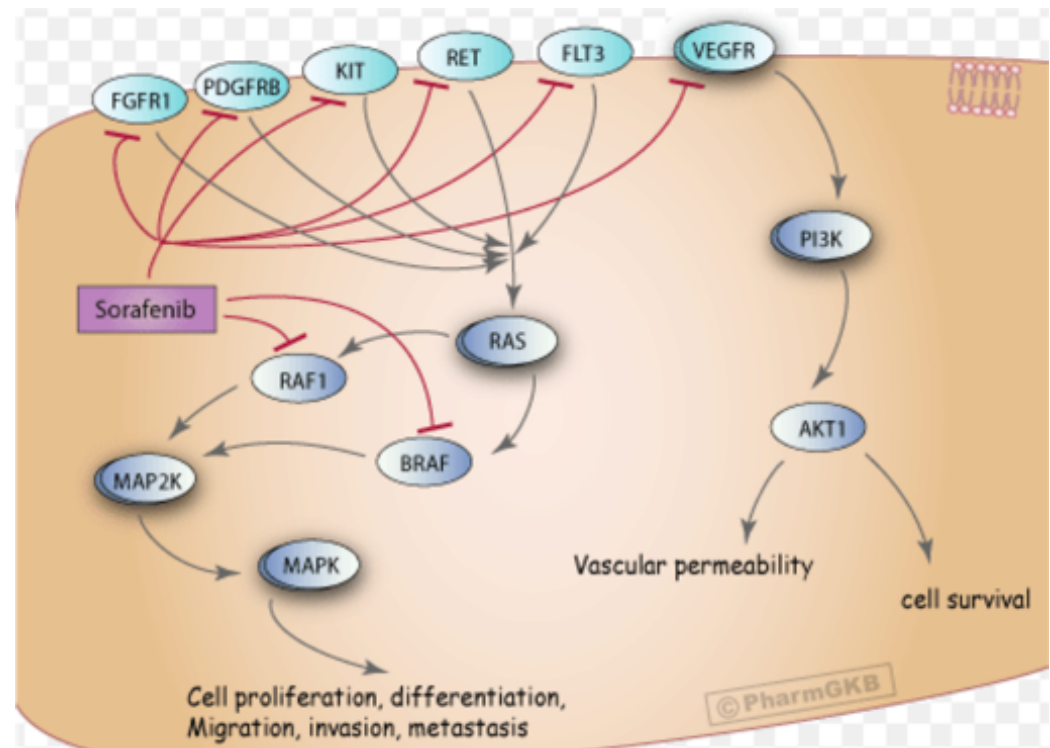
HEPATOCELLULAR CARCINOMA HCC RESISTENCE TO MULTI KINASE INHIBITOR



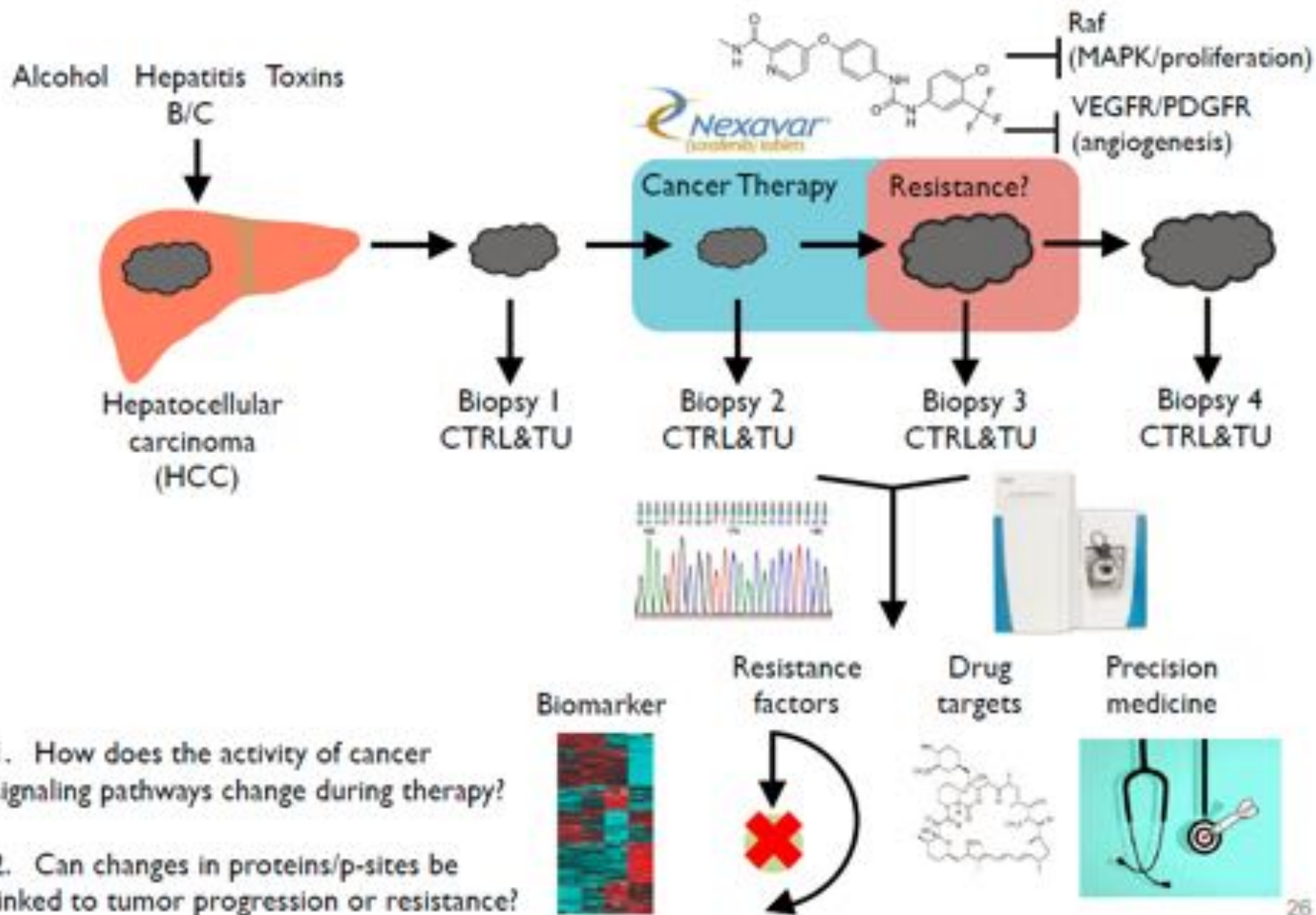
750,000 HCC new cases per year



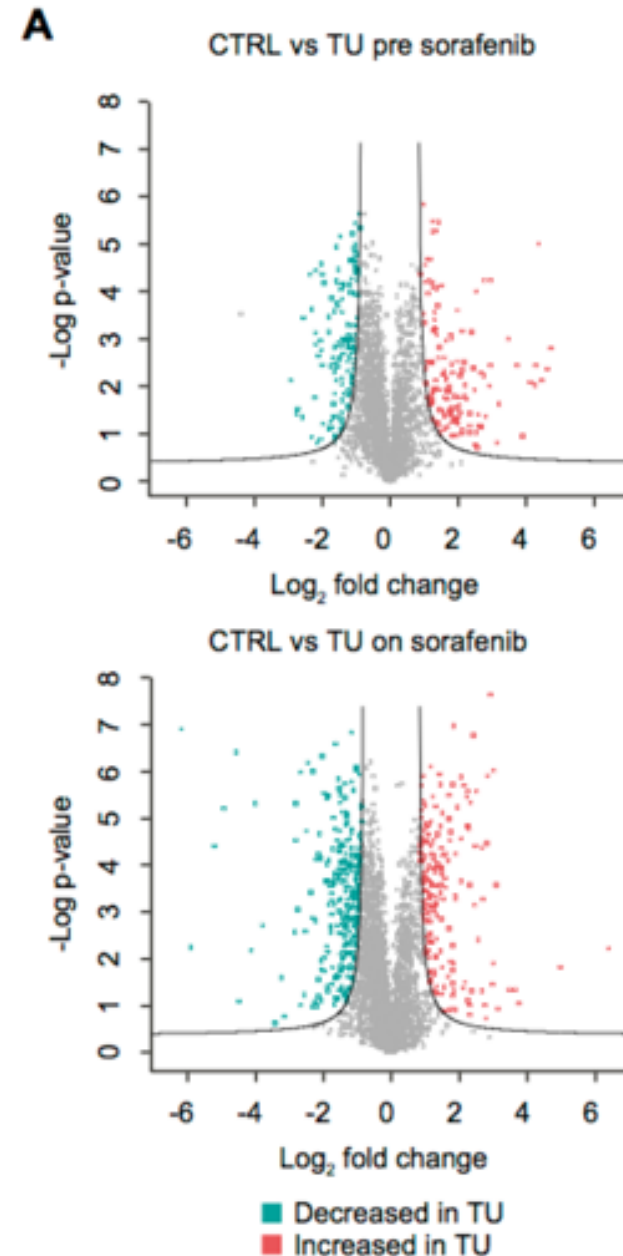
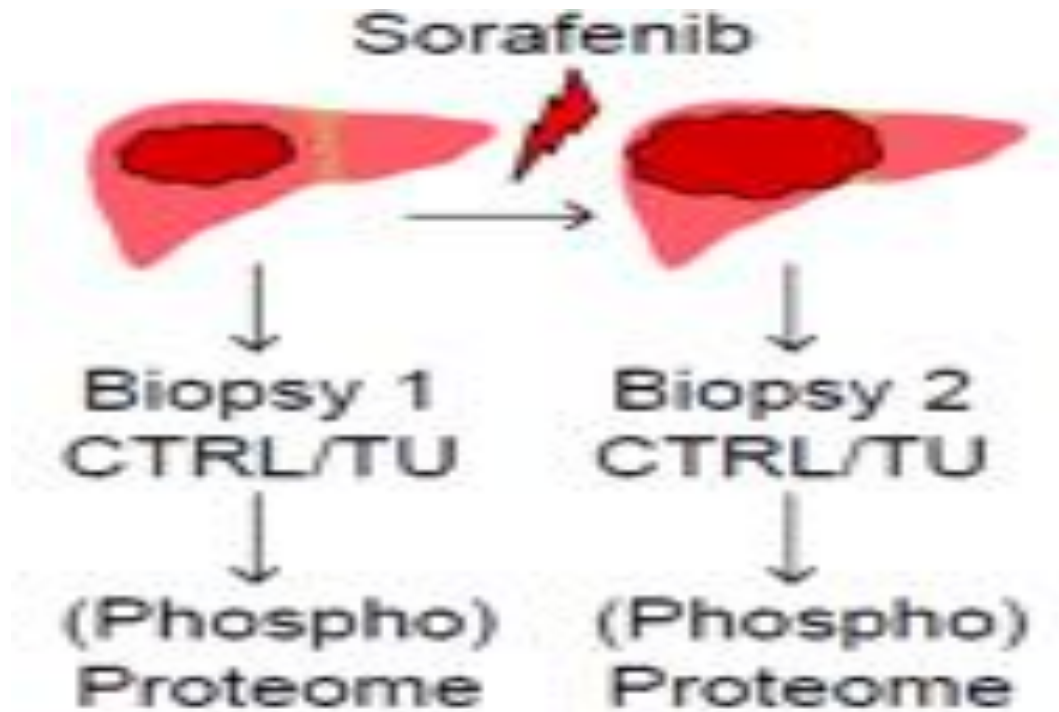
Poor prognosis for patients : 1y survival (liver transplants excl)
Sorafenib median patient survival by 3 months



«Hall – Heim» Basel translational research: longitudinal studies allows to trace in patients evasive cancer drug resistance



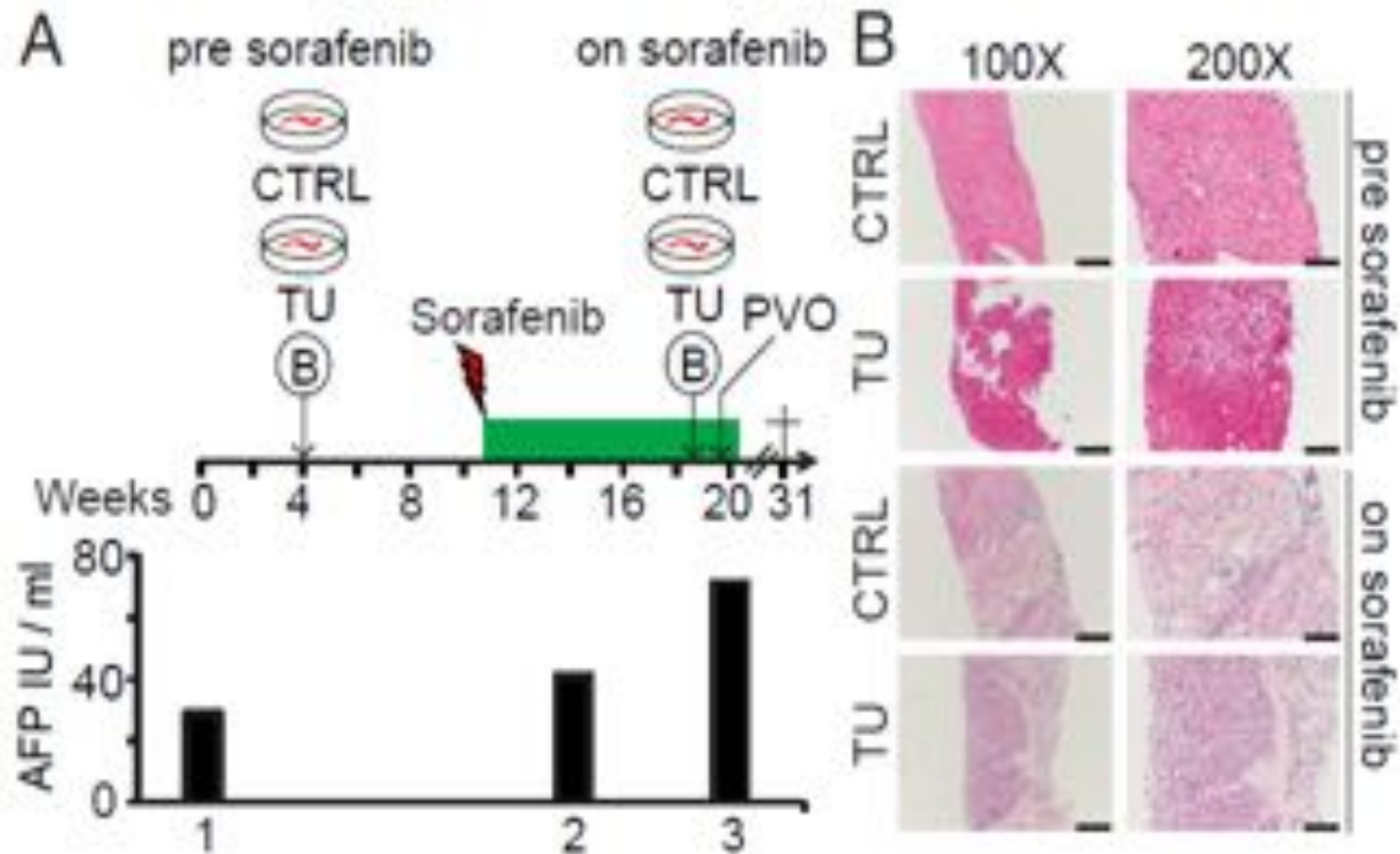
Translational Research: quantitative phosphoproteomics allows to trace evasive cancer drug resistance



liver cancer tumour vs healthy part of the patient liver

Drug cocktail can be translated to the clinic for precision therapy upon quantitative phosphoproteomics of patient needle biopsies (not resected tumours)

Translational Research: quantitative phosphoproteomics allows to trace evasive cancer drug resistance



FROM BENCH TO BEDSIDE AND BACK

Fig. 2. Clinical data of the sorafenib-treated HCC patient. (A) Clinical history of the sorafenib-treated HCC patient. The green bar indicates sorafenib treatment. PVO, portal vein occlusion. (B) H&E staining of HCC patient biopsies. (Scale bars: 100x magnification, 200 μ m; 200x magnification, 100 μ m.)

Translational Research: quantitative phosphoproteomics allows to trace evasive cancer drug kinase inhibitor resistance

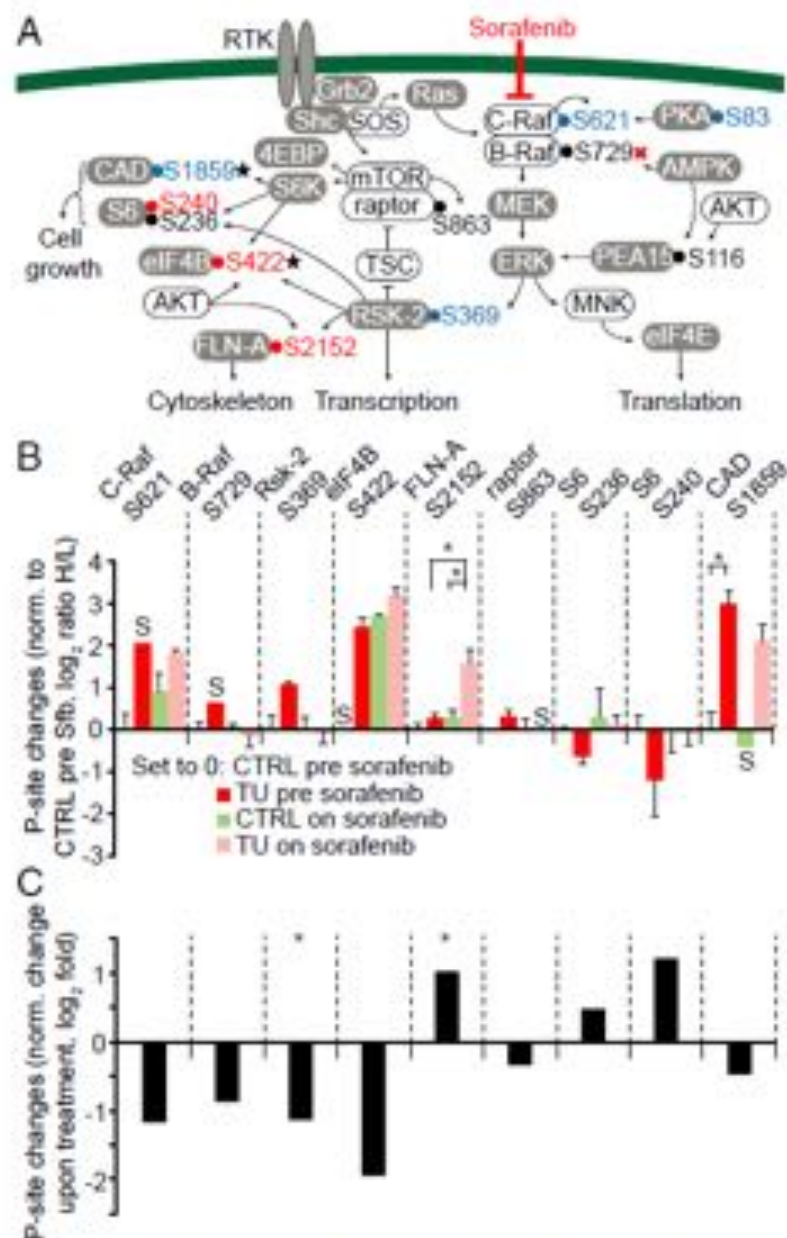
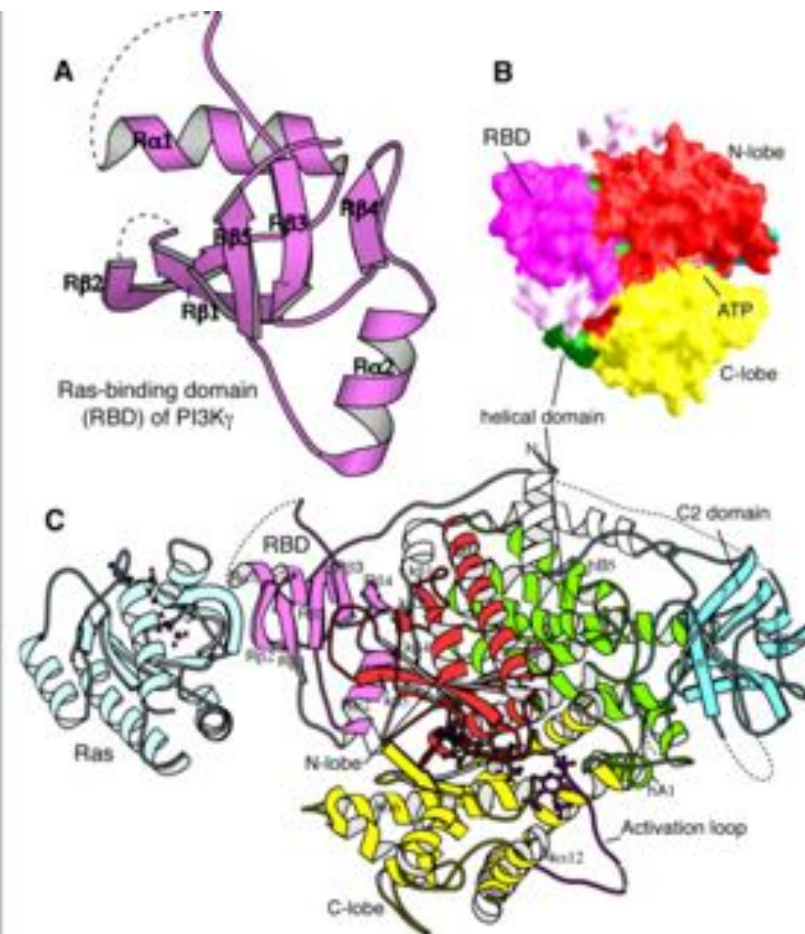


Fig. 5. Changes in MAPK pathway (34–37) activity upon sorafenib treat-



FROM BENCH TO BEDSIDE AND BACK

First ever live phosphoproteomic (SILAC validated) analyses on recurrent patient liver biopsies demonstrating that sorafenib did inhibit MAPK within the patient tumour but fail to inhibit/activated growth signal downstream !

MN. Hall and M Heim labs, by Dazert E et al. (2016) Proc Nat Acad Sci 113: 1381-1386

Translational Research: challenges at the wake of
to tracing evasive cancer drug resistance from patient tumours



CANCER PATIENT PERSONALIZED INNOVATIVE MEDICINE WILL BE SOLVED BY BIOPSY (MOLECULAR PATHOLOGY SCREENS) AND NOT MERELY BY DNA/RNA SEQ !

(my personal opinion)

Future : suitable medicines (drug cocktails) can be translated to the clinic for precision therapy upon quantitative phosphoproteomics of patient biopsies

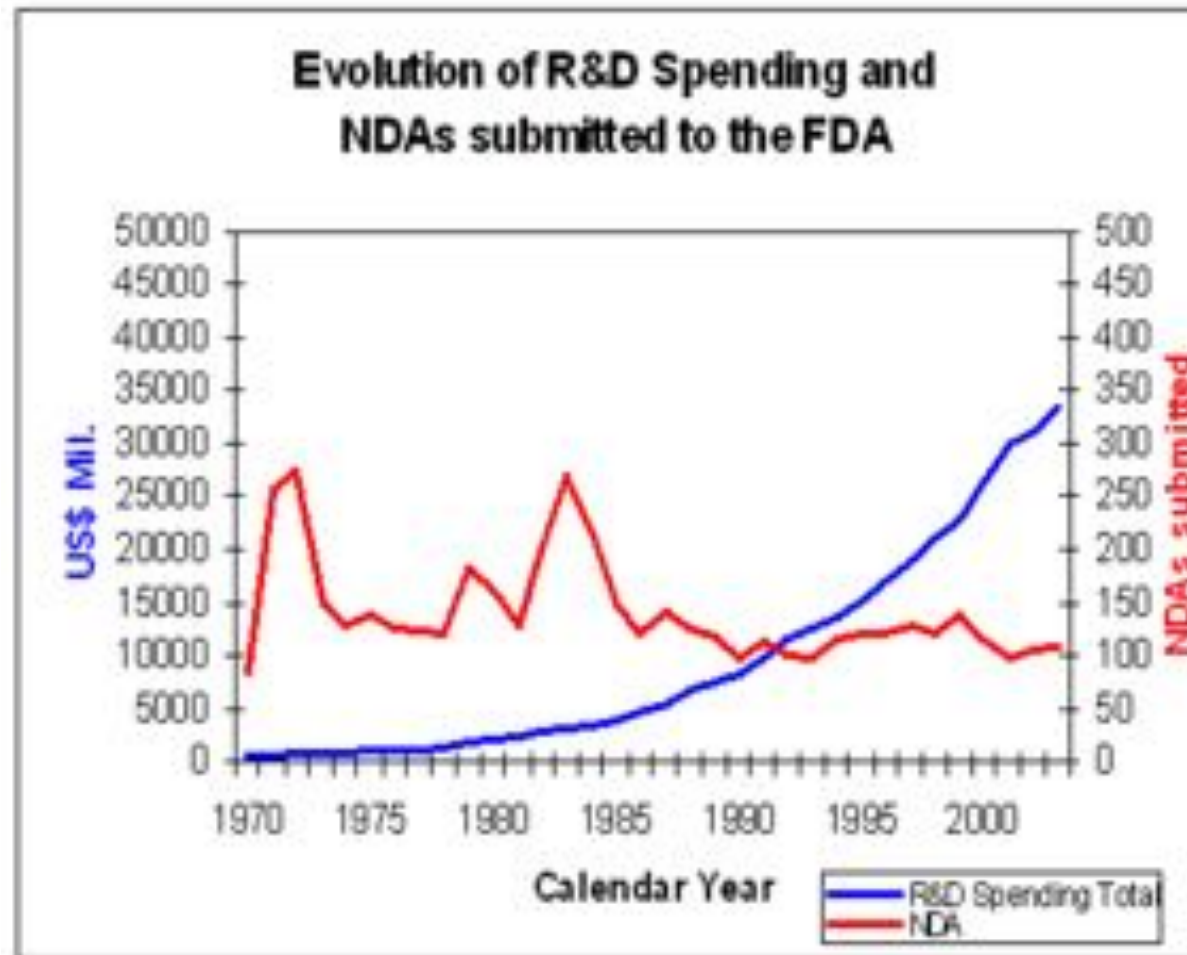
**SOLID TUMOR CANCER METASTASES MAY NEVER BEEN CURED FULLY ERADICATED,
HOWEVER HOPEFULLY REDUCED TO A CHRONIC DISEASE !**



- Translational research is meant to convert the valley of death into the garden of Eden ? More efficient healthcare ?



Complexity increases_ crossing the valley of death ?

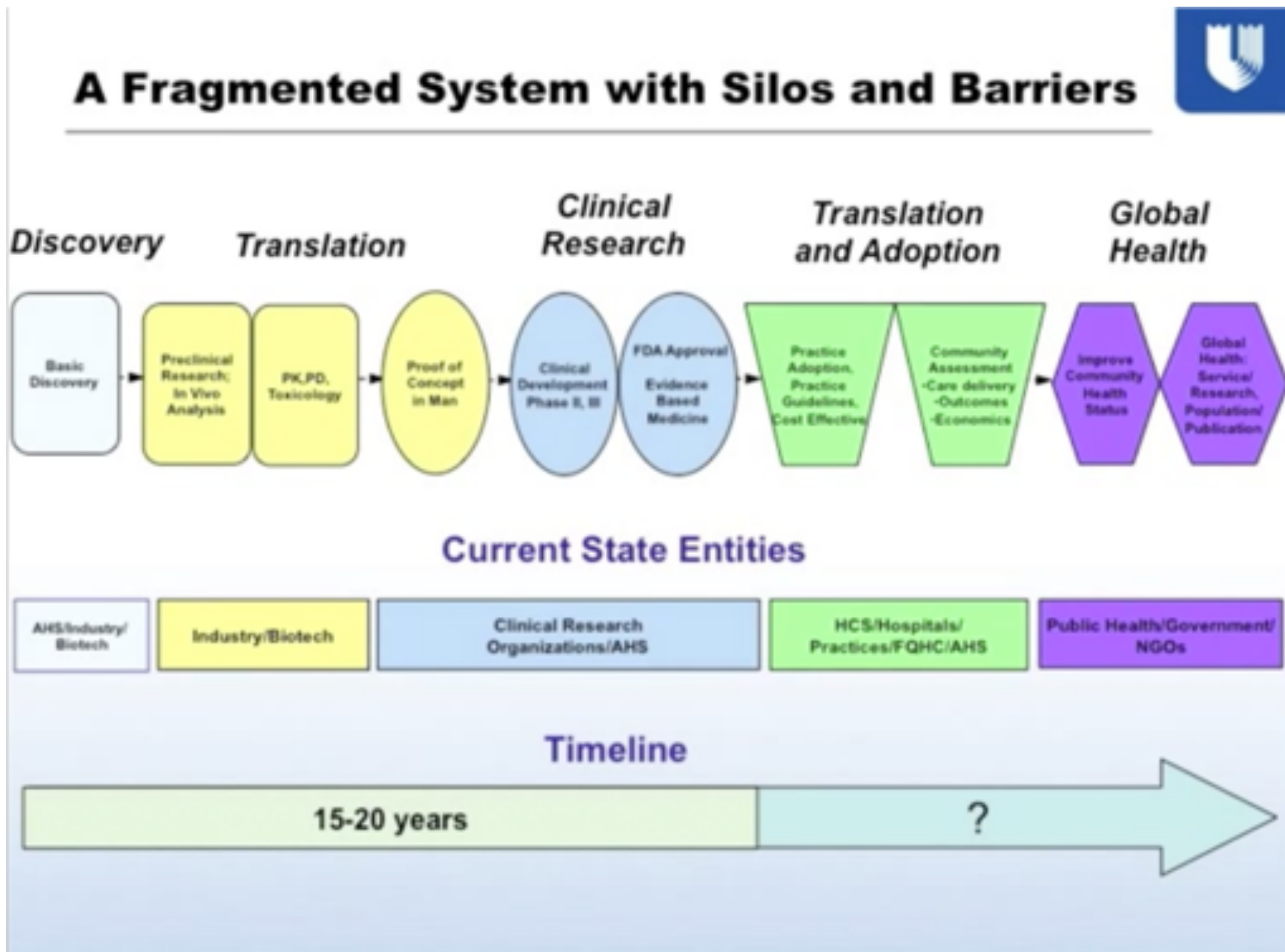


<http://www.vishnoba.de/ficpp/imm.htm>

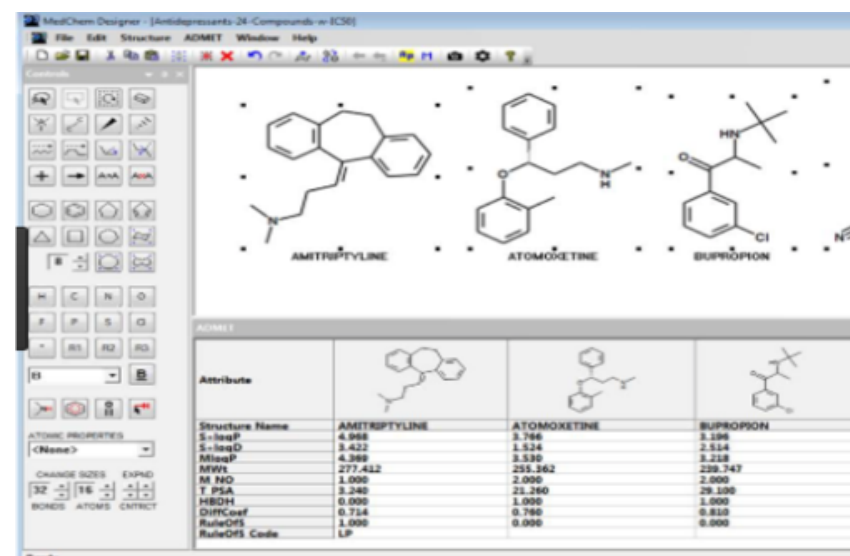
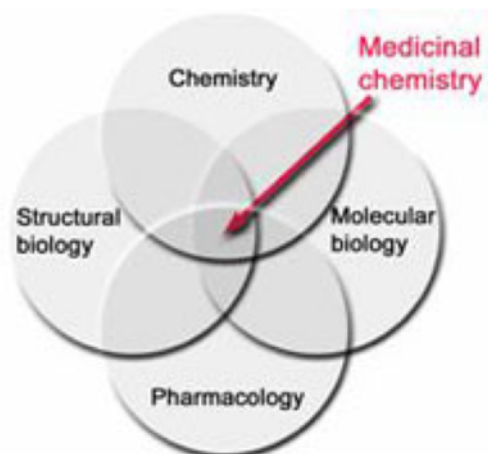
- Investment of Pharma has been continuously increasing
- This did not translate into a parallel increase of new drug applications (NDA) to regulatory authorities (FDA)

TRANSLATIONAL RESEARCH : TRANSLATE SCIENCE TO THE CLINIC AND BRING NEW THERAPIES TO PATIENTS

Traditional healthcare research _ ancient research programs a silo fighting recipe !



Translational research – challenges and critics



Biomedical research scientists (the traditional team including medicinal chemists, pharmacologists and mol biologists) heavily focused on animal pharm models for validating an innovative medicine ??



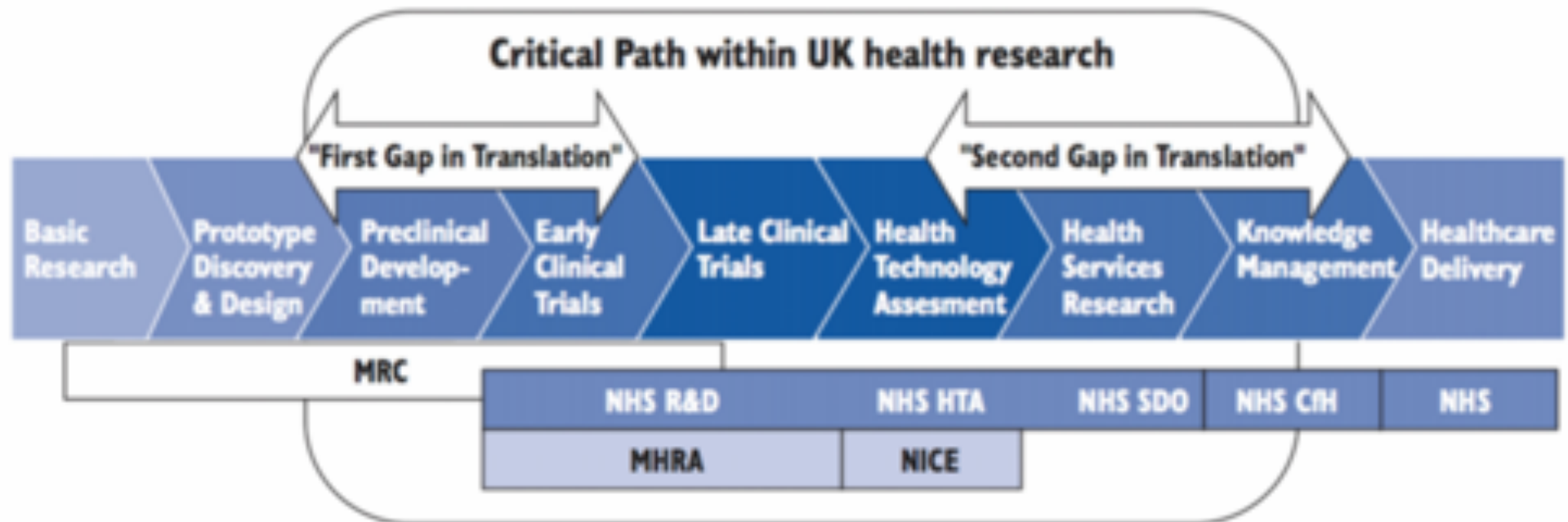
- Making unrealistic promises for quick discoveries and cures may damage the credibility of science in the eyes of the patients (info vs intox)



Translational research : the road blocks



From bench to bedside and back – healthcare improvement ?

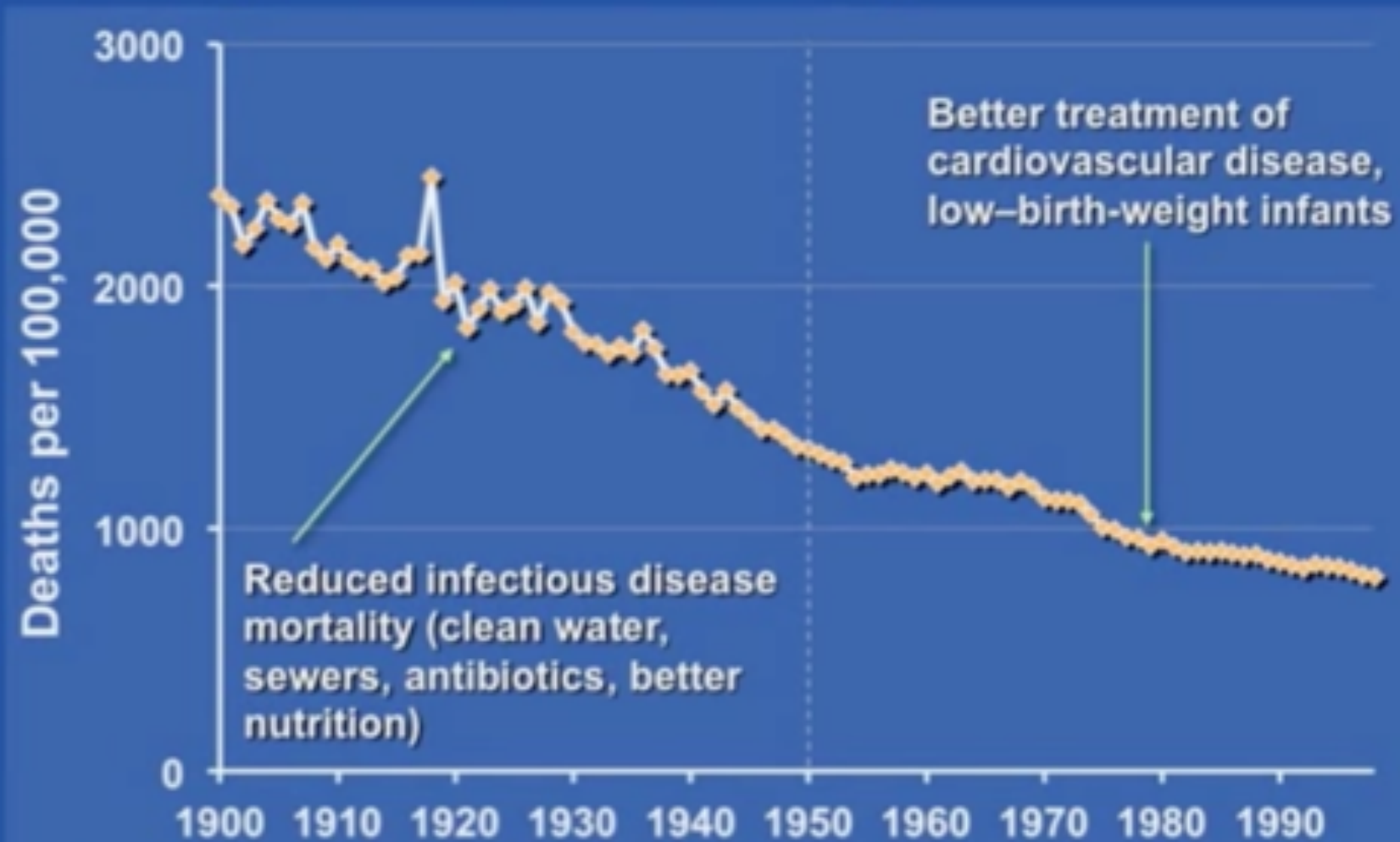


PATIENTS SUPPORTS, GUIDES TRANSLATIONAL RESEARCH AT MAINLY TWO STEPS OF THE DEVELOPMENT OF INNOVATIVE MEDICINES

20th century healthcare remit _ the good news
How is your 21st century research going to keep up with this trend ?



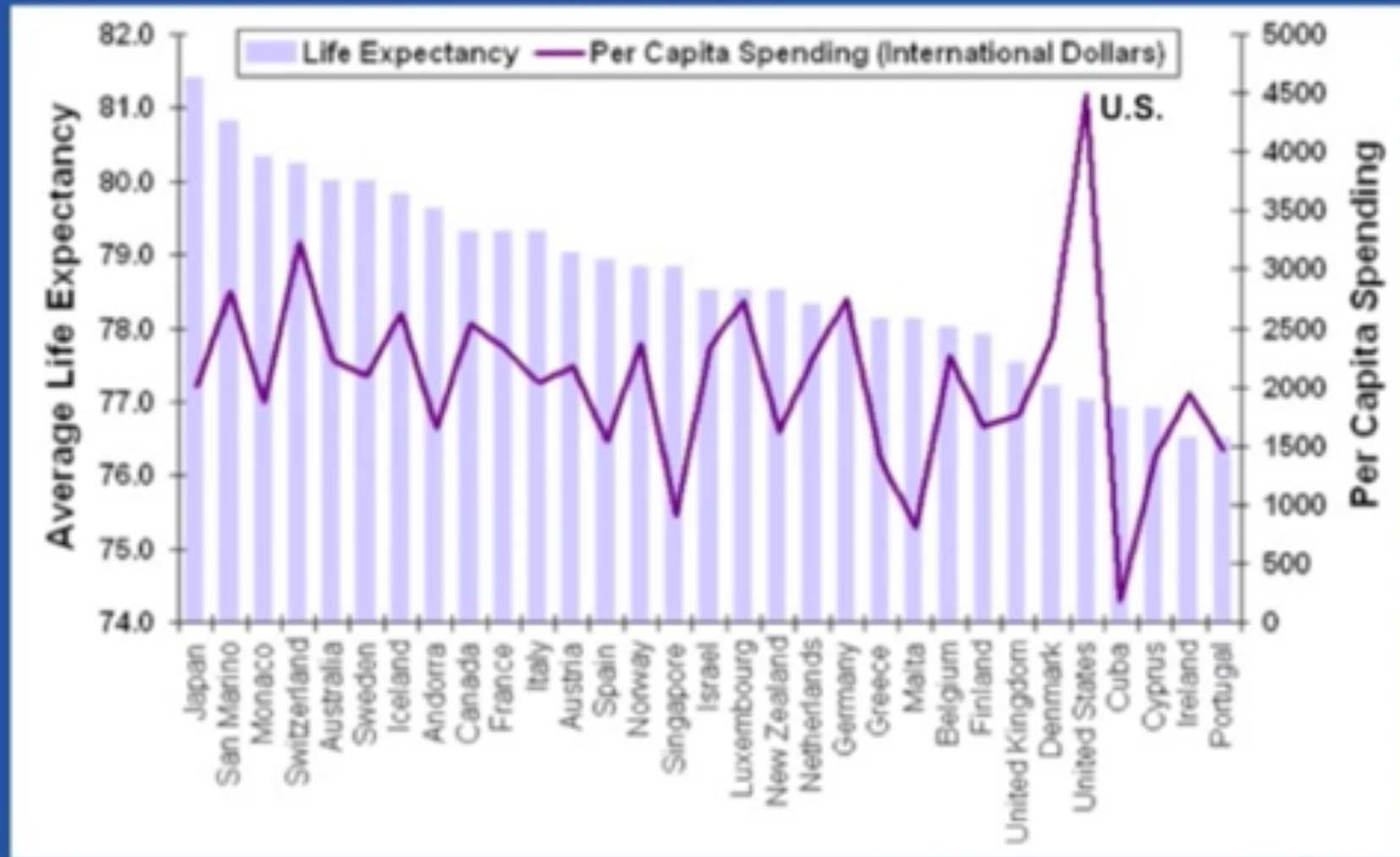
Mortality in the 20th Century



At what costs : healthcare costs are exploding _ the bad news



The Cost of a Long Life



Translational oncology research - cell therapies

CAR-T cells @ Kymriah



- the development of genetically engineered cells that target tumor antigens is one of the most promising recent studies in immuno-oncology.
- harnessing the patient's own immune system to target and kill cancer cells (eg chimeric antigen receptor (CAR) T cells) modified to recognize tumor antigens have shown remarkable results in clinical trials. Further studies will follow.

BREAKING NEWS



FDA approved for Acute lymphocytic leukemia (ALL), a fast-growing cancer of lymphocyte-forming cells called *lymphoblasts*. Cost CHF460.000.— **Tox warning:** cytokine storm Actemra tocilizumab as « antidote »



WHO 2050 - 10 MILLION DEATH
TOLL EACH YEAR BY 2050
ATTRIBUTABLE TO
ANTIMICROBIALS MULTI
RESISTANCE : A GLOBAL SCALE
FAILURE

21st century healthcare challenge_the
bacterial resistance pandemic

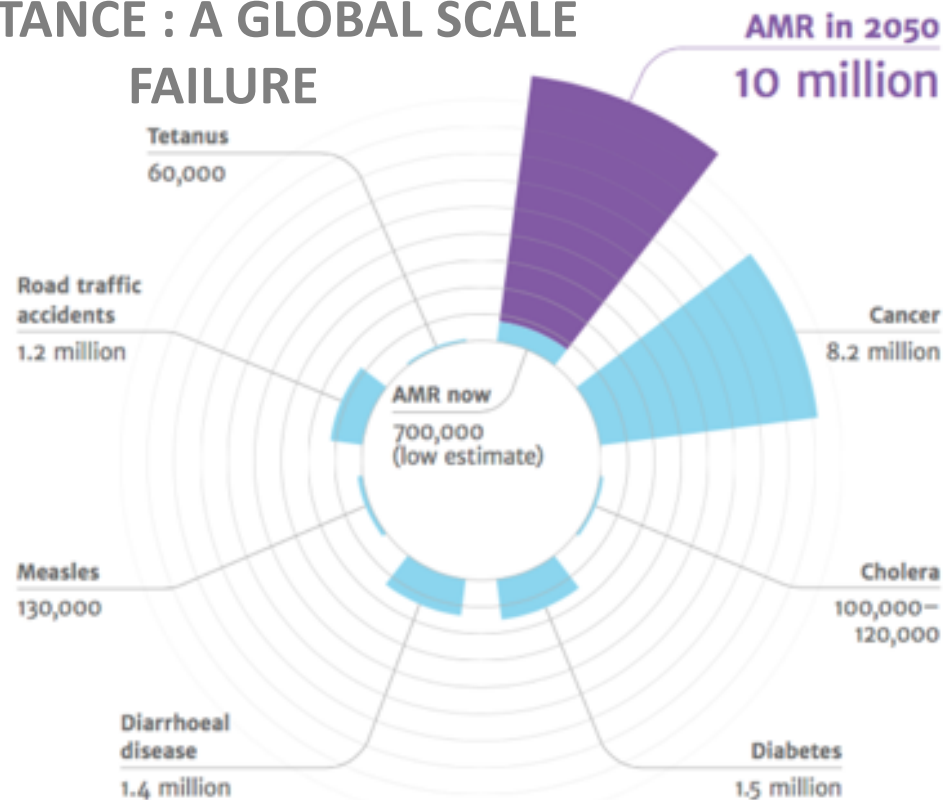


REPORT TO THE
SECRETARY-GENERAL
OF THE UNITED NATIONS



World Health
Organization

APRIL 2019



Sources:

Diabetes: www.who.int/mediacentre/factsheets/fs333/en/ Cancer: www.who.int/mediacentre/factsheets/fs333/en/
Cholera: www.who.int/mediacentre/factsheets/fs333/en/ Diarrhoeal disease: www.who.int/mediacentre/factsheets/fs333/en/
Measles: www.who.int/mediacentre/factsheets/fs333/en/ Road traffic accidents: www.who.int/mediacentre/factsheets/fs333/en/
Tetanus: www.who.int/mediacentre/factsheets/fs333/en/

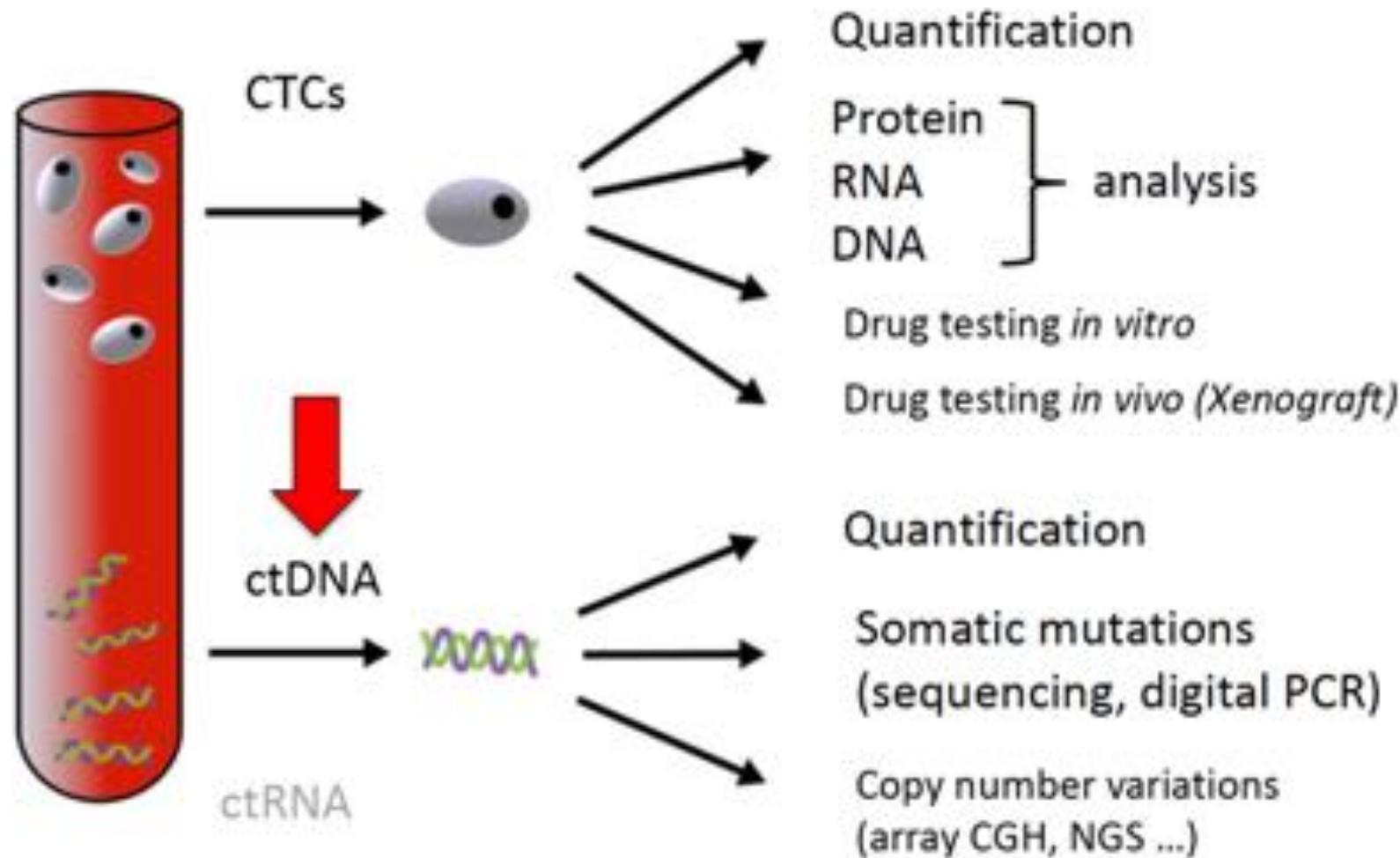
Review on
Antimicrobial
Resistance



Biomarker discovery_liquid biopsies_translational research meets with personalized healthcare



liquid biopsies : what is in there ? Overcoming tumor heterogeneity !



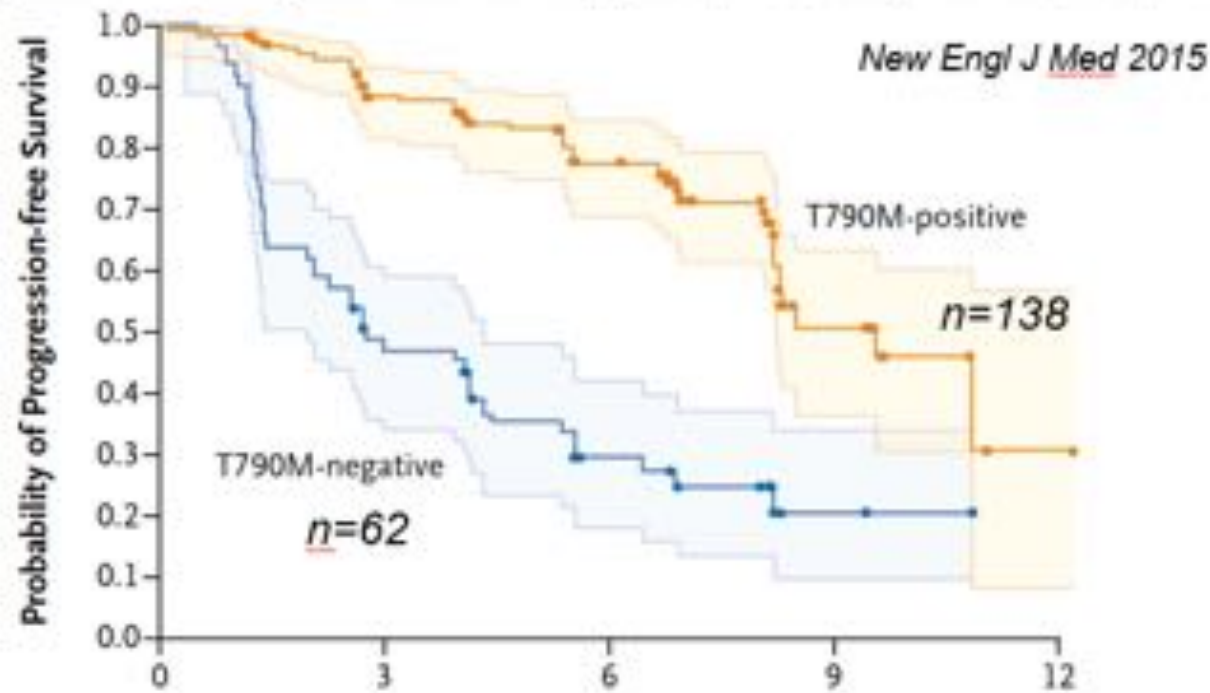
CTCs: circulating tumor cancer cells (glioma excepted?). Solid biopsies are frustrating as they rely on the evasive cancer drug resistance of the primary tumor !

CTCs cluster profiling can be used non invasively to monitor drug susceptibility in patients !



AZD9291 in EGFR Inhibitor-Resistant Non-Small-Cell Lung Cancer

Pasi A. Jänne, M.D., Ph.D., James Chih-Hsin Yang, M.D., Ph.D., Dong-Wan Kim, M.D., Ph.D.,



Osimertinib (3rd generation TKI):

- Partial or full remission in ca. 60% of patients
- Approved for the resistant NSLC

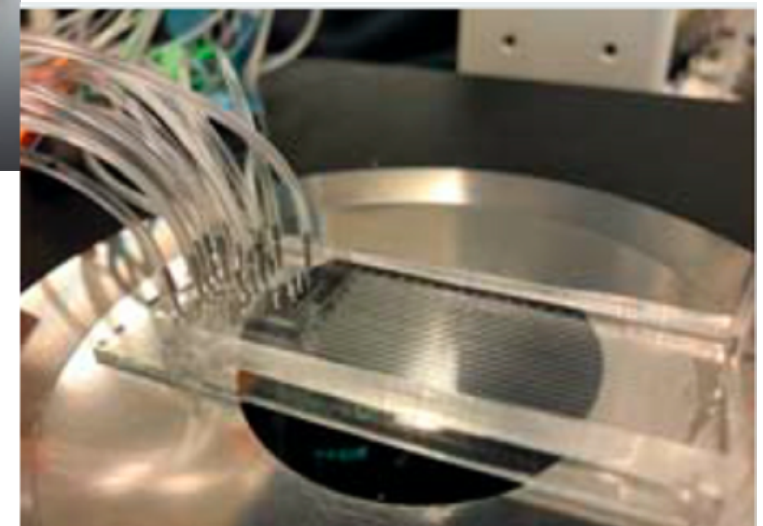
Lung cancer is the major cause of cancer death in the world while non small cell lung cancer (NSCLC) accounts approx. 85% of all lung cancer diagnosis. Approximately 50% of non-small cell lung cancer (NSCLC) patients who develop resistance to inhibitors of the epidermal growth factor receptor (EGFR) have acquired a second mutation, T790M.

Biomarker discovery_early front loading for preventive medicine and cohort stratification in clinical research

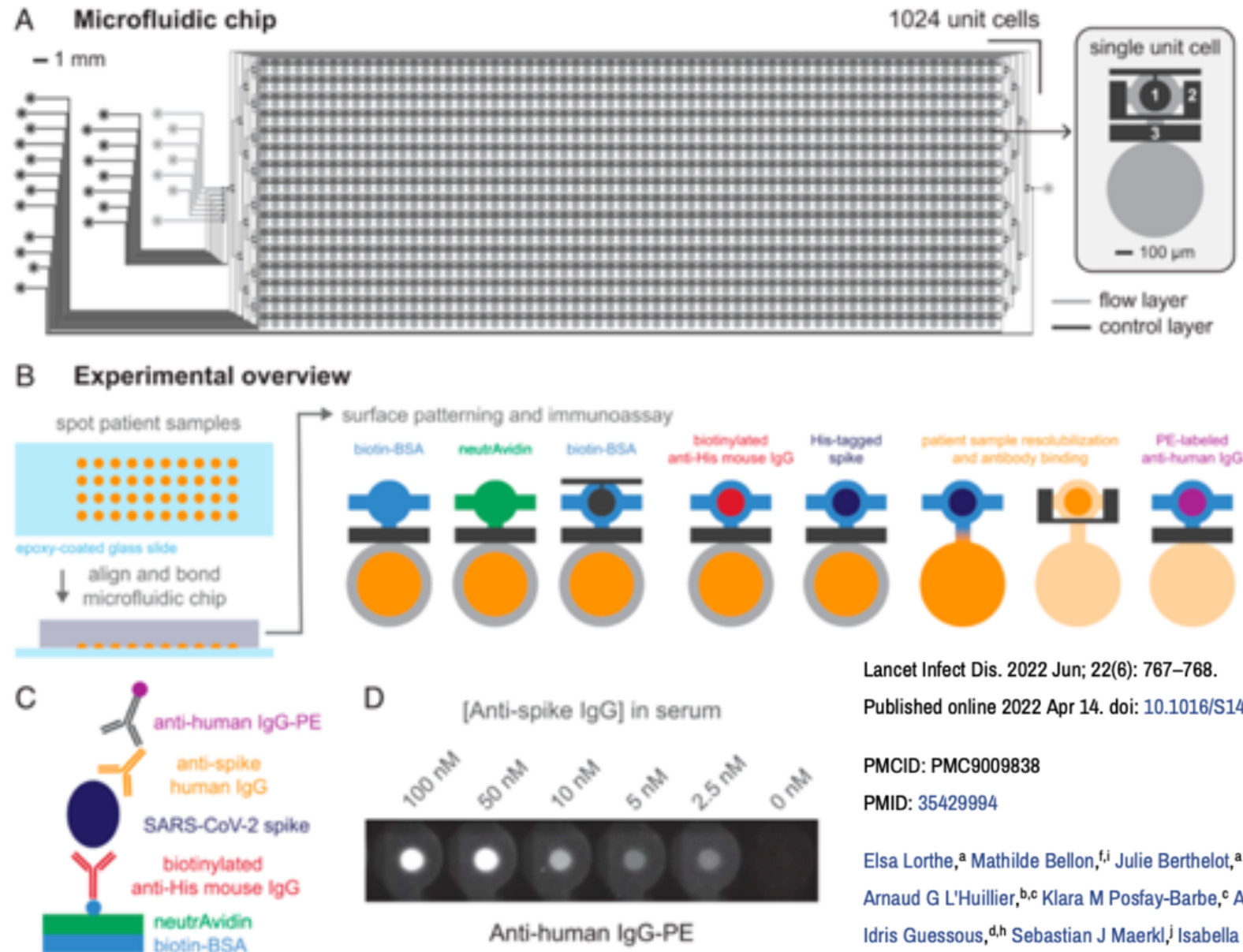


Diabète & Nutrition www.diabetsnutrition.ch	HbA1c %	Glycémie mmol/L
	4,4	4,4
	4,7	4,9
	5,0	5,4
	5,3	5,8
	5,6	6,3
	5,9	6,8
	6,0	7,0
	6,2	7,3
	6,5	7,8
	7,0	8,6
	7,2	8,9
	7,5	9,4
	7,7	9,7
	8,0	10,2
	8,3	10,6
	8,6	11,1
	9,0	11,8
	9,2	12,1
	9,8	13,0
	10,0	13,4
	10,4	14,0
	11,0	14,9
	12,0	16,5

Glycosylated hemoglobin HbA1c -microfluidic an nanoimunoassay



Biomarker discovery by Nialabs in preventive medicine eg SarsCoV2 screens in community/herd immunity



Lancet Infect Dis. 2022 Jun; 22(6): 767–768.

Published online 2022 Apr 14. doi: [10.1016/S1473-3099\(22\)00267-5](https://doi.org/10.1016/S1473-3099(22)00267-5)

PMCID: PMC9009838

PMID: 35429994

Elsa Lorthe,^a Mathilde Bellon,^{f,i} Julie Berthelot,^a Grégoire Michielin,^j Arnaud G L'Huillier,^{b,c} Klara M Posfay-Barbe,^c Andrew S Azman,^{a,g,k} Idris Guessous,^{d,h} Sebastian J Maerkl,^j Isabella Eckerle,^{b,e,f,i} Silvia Stringhini,^{a,h,i} and SEROCov-Schools Study Group, on behalf of the



Mod Pathol 36 (2023) 100088

MODERN PATHOLOGY



Journal homepage: <https://modernpathology.org/>

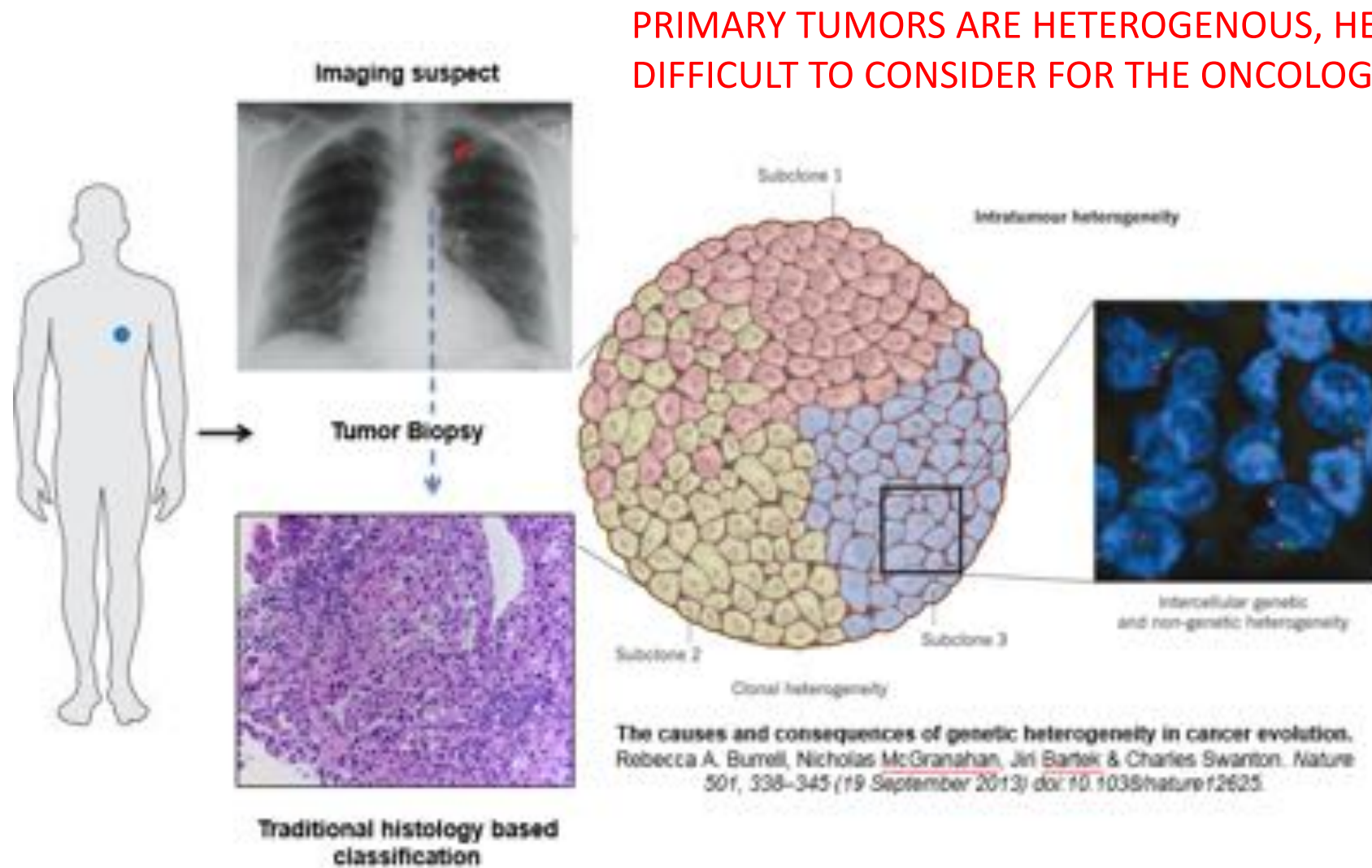
Research Article

MarrowQuant 2.0: A Digital Pathology Workflow Assisting Bone Marrow Evaluation in Experimental and Clinical Hematology

Rita Sarkis^{a,b,c}, Olivier Burri^d, Claire Royer-Chardon^e, Frédérica Schyrr^a, Sophie Blum^a, Mariangela Costanza^f, Stephane Cherix^g, Nathalie Piazzon^e, Carmen Barcena^{e,h}, Bettina Bisig^e, Valentina Nardiⁱ, Rossella Sarro^{e,j}, Giovanna Ambrosini^k, Martin Weigert^l, Olivier Spertini^f, Sabine Blum^f, Bart Deplancke^m, Arne Seitz^d, Laurence de Leval^e, Olaia Naveiras^{a,j,*}

^a Laboratory of Regenerative Hematopoiesis, Institute of Bioengineering & ISREC, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland; ^b Department of Biomedical Sciences, University of Lausanne (UNIL), Lausanne, Switzerland; ^c Laboratory of Systems Biology and Genetics, Institute of Bioengineering, School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland; ^d Biomedicine and Optics Core Facility, School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne.

Tumor heterogeneity _ patient “liquid” biopsies and omics



VARIOUS CTCs CLUSTERS MAY ORIGINATE FROM ALL THE DIFFERENT PARTS OF THE PRIMARY TUMOR !!

Big data analyses – individual biomarker discovery



From bench to bedside and back – will big data overcome patient heterogeneity ! ?



GLOBAL LEADER IN DATA-DRIVEN MEDICINE

POWER YOUR CLINICAL GENOMIC TEST

== with ==

SOPHiA™

THE COLLECTIVE ARTIFICIAL INTELLIGENCE FOR DATA-DRIVEN MEDICINE

Watch the video

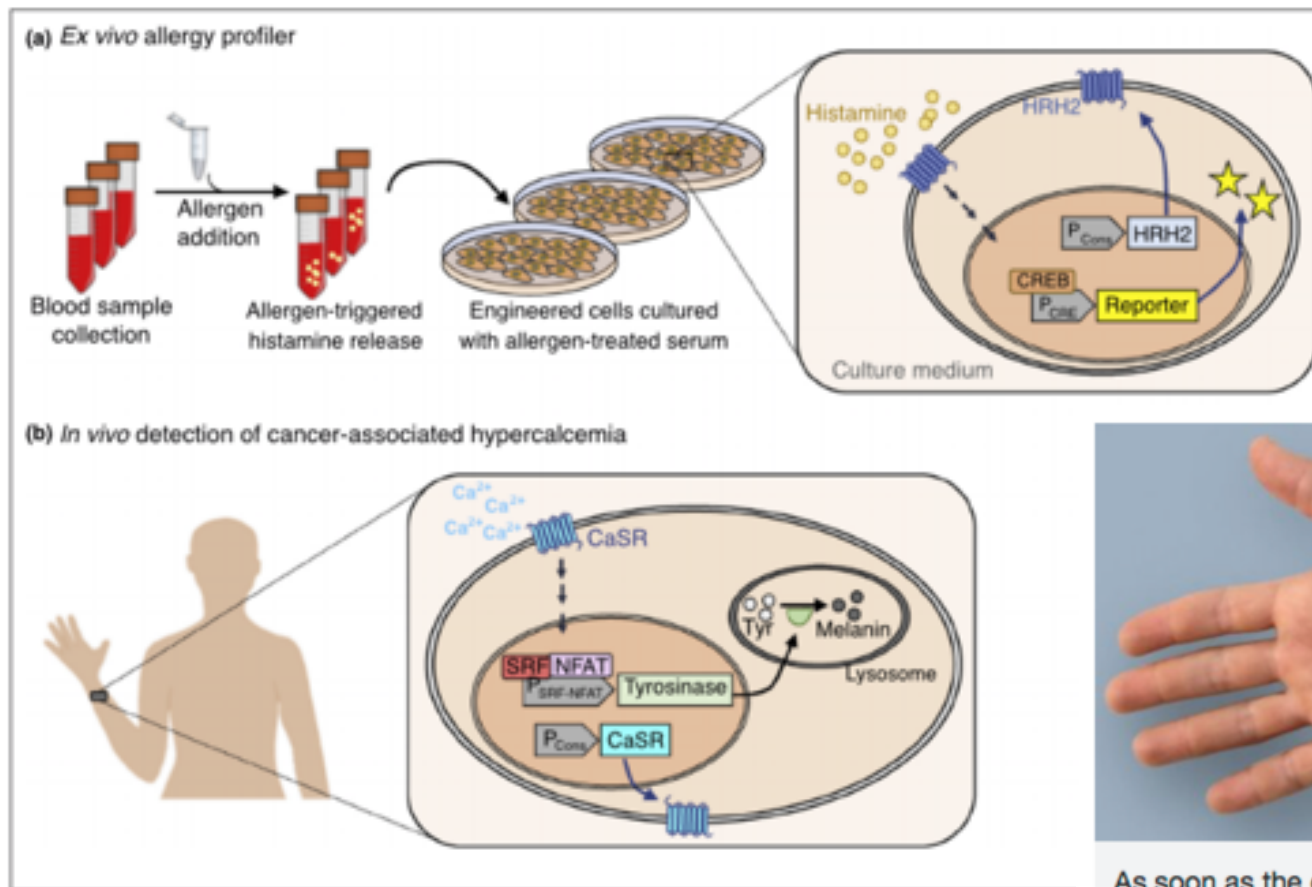
Metric	Value
Countries	53
Hospitals	334
Patients Tested	127'000

**WITH SUPPORT OF DNA, RNA, PROTEIN DRIVEN 2.0 MEDICINE,
DATA SCIENTISTS, AI-STARTUPS, LARGE PHARMACEUTICALS ?**

Early front loading of disease enabling biomarkers



Figure 2



repurposing
fibroblasts as living
biomarkers



As soon as the calcium level exceeds a particular threshold over a longer period of time, an implant inserted under the skin triggers the production of melanin. This causes a mole to form. (Simulated montage)

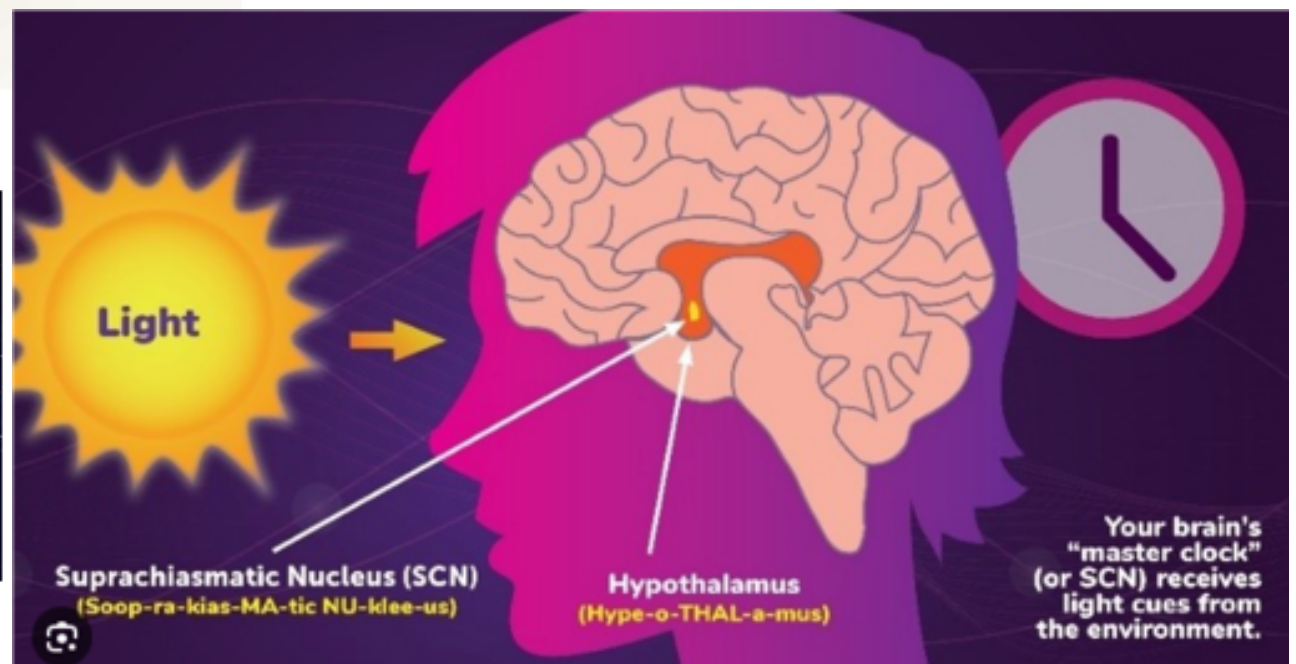
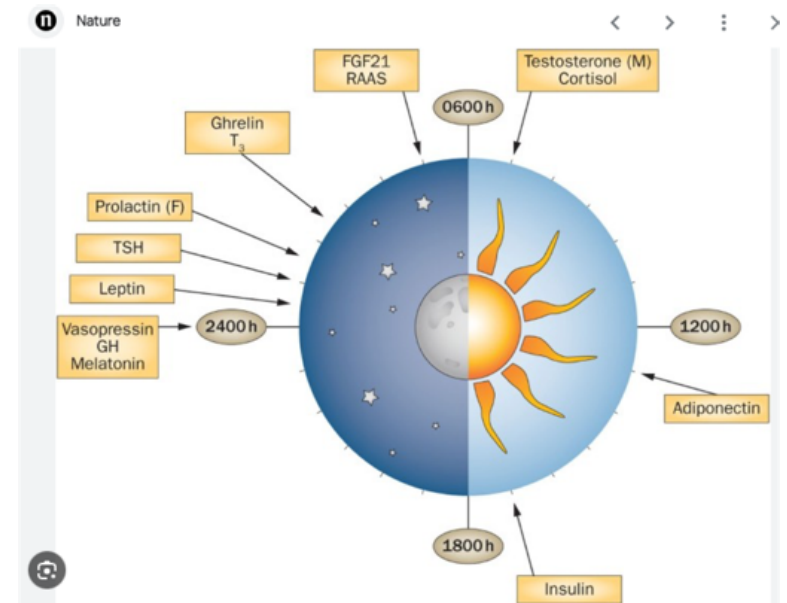
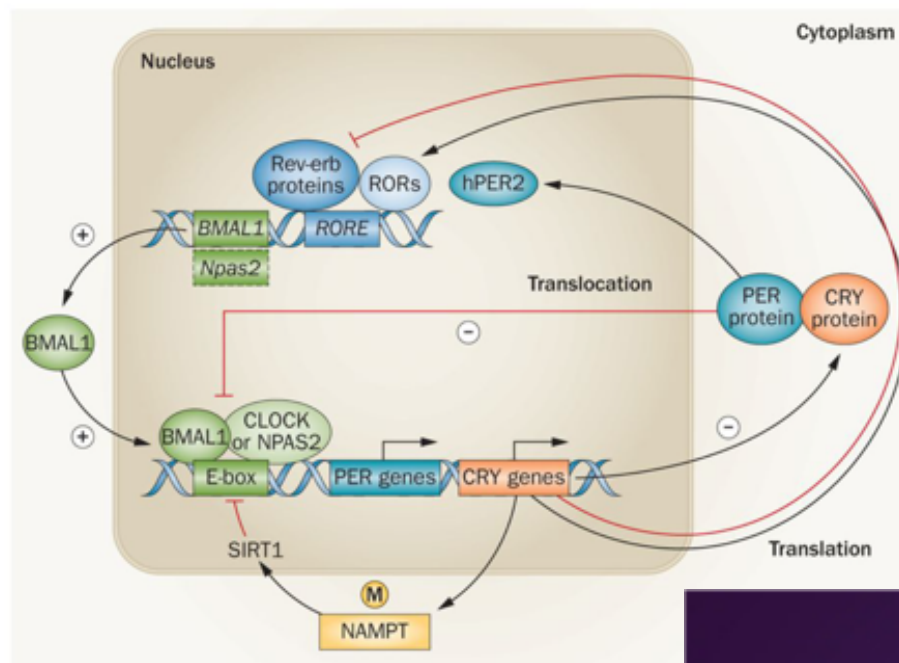
Applications of mammalian synthetic biology in diagnostics. **(a)** Ex vivo allergy profiler. Whole blood samples are treated which then trigger histamine release by basophils in samples from allergic patients. A small volume of serum is added encoding the histamine sense-and-response device, which will diagnose an allergy by expressing a fluorescent protein is sensed by the ectopically expressed HRH2 receptor, which triggers an endogenous signaling cascade that culminates in the expression of a reporter protein. **(b)** In vivo detection of cancer-associated hypercalcemia. Ectopically expressed CaSR receptor senses sustained hypercalcemia and triggers endogenous signaling cascades that culminate in the expression of the tyrosinase enzyme by a synthetic promoter (P_{SRE-NFAT}) containing binding sites for both serum response factor and NFAT transcription factors. Tyrosinase converts tyrosine to melanin inside lysosomes. Designer cells encoding all device components could be subcutaneously implanted in patients with hypercalcemia to diagnose cancer-associated hypercalcemia.

Prof Martin Fussenegger et al ETHZ-Systems biology D-BSSE

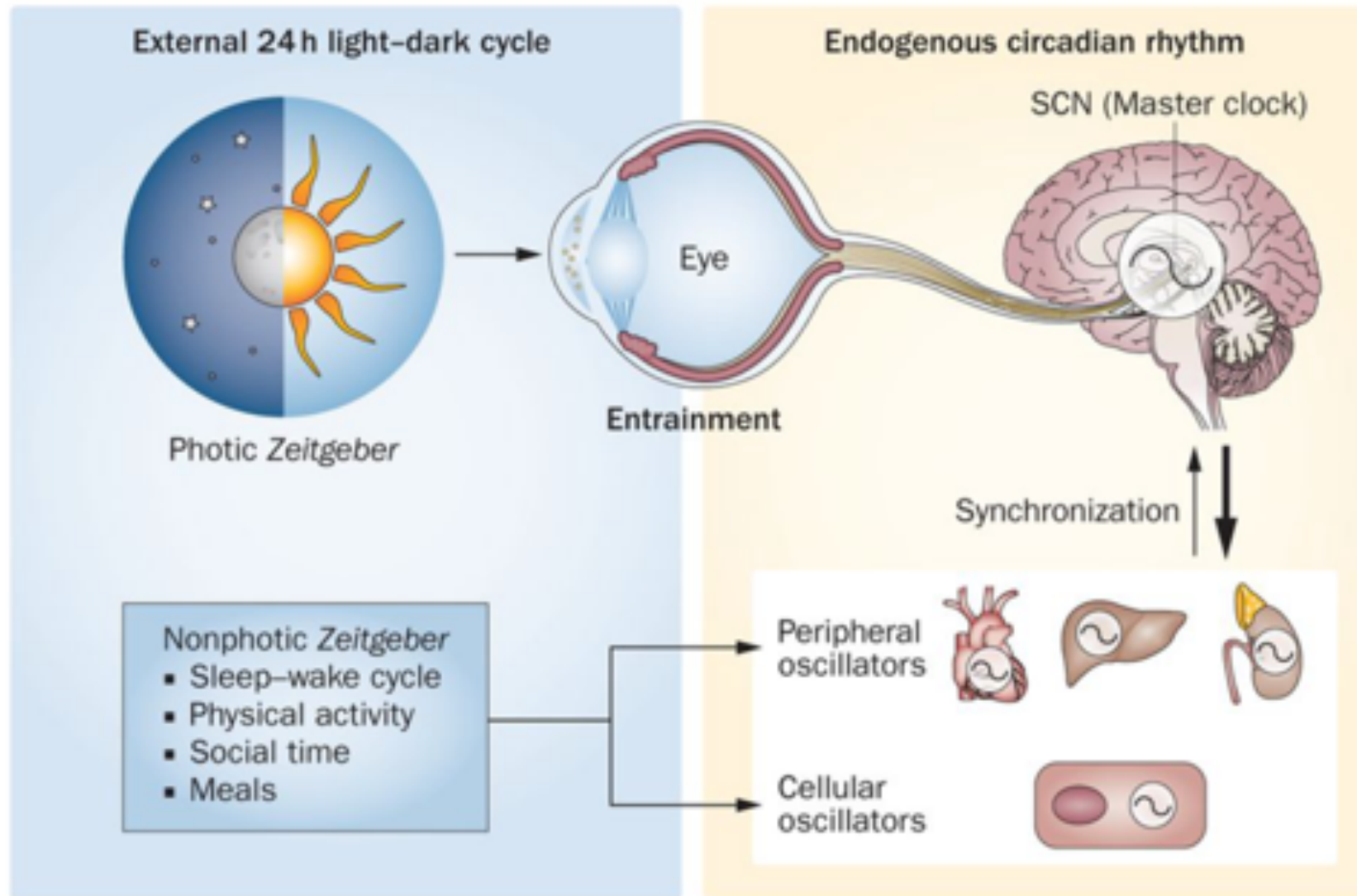
Chronobiology : feedforward/backward gene regulatory loops - the underlying molecular mechanisms



From: Clocking in: chronobiology in rheumatoid arthritis



Circadian clock oscillator : the planet earth rotation : yet chronotherapy has not yet really reached the clinics – why ?

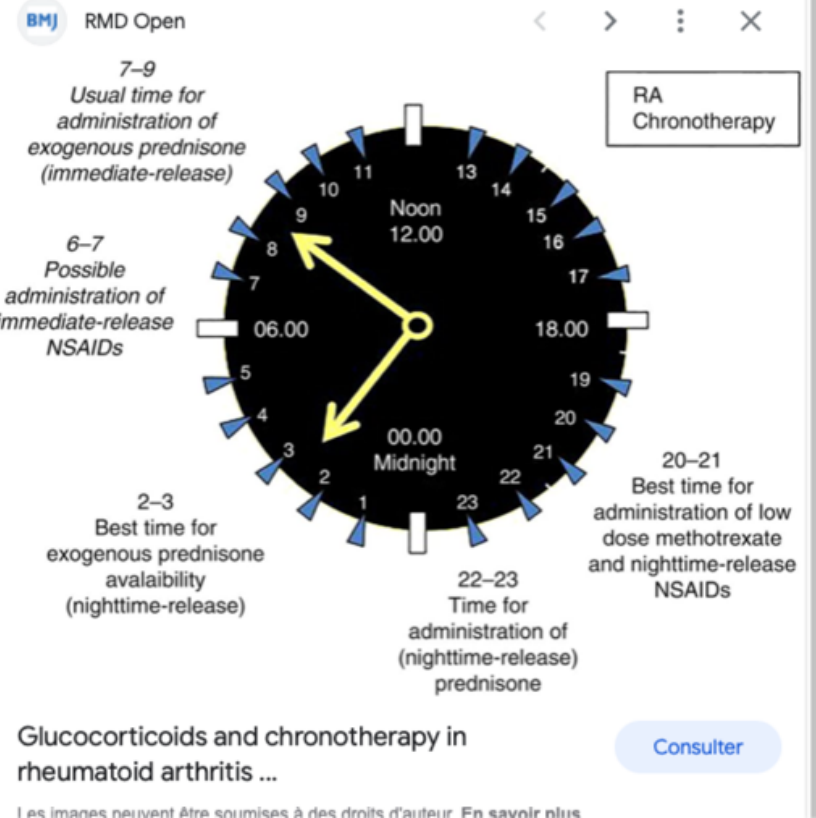
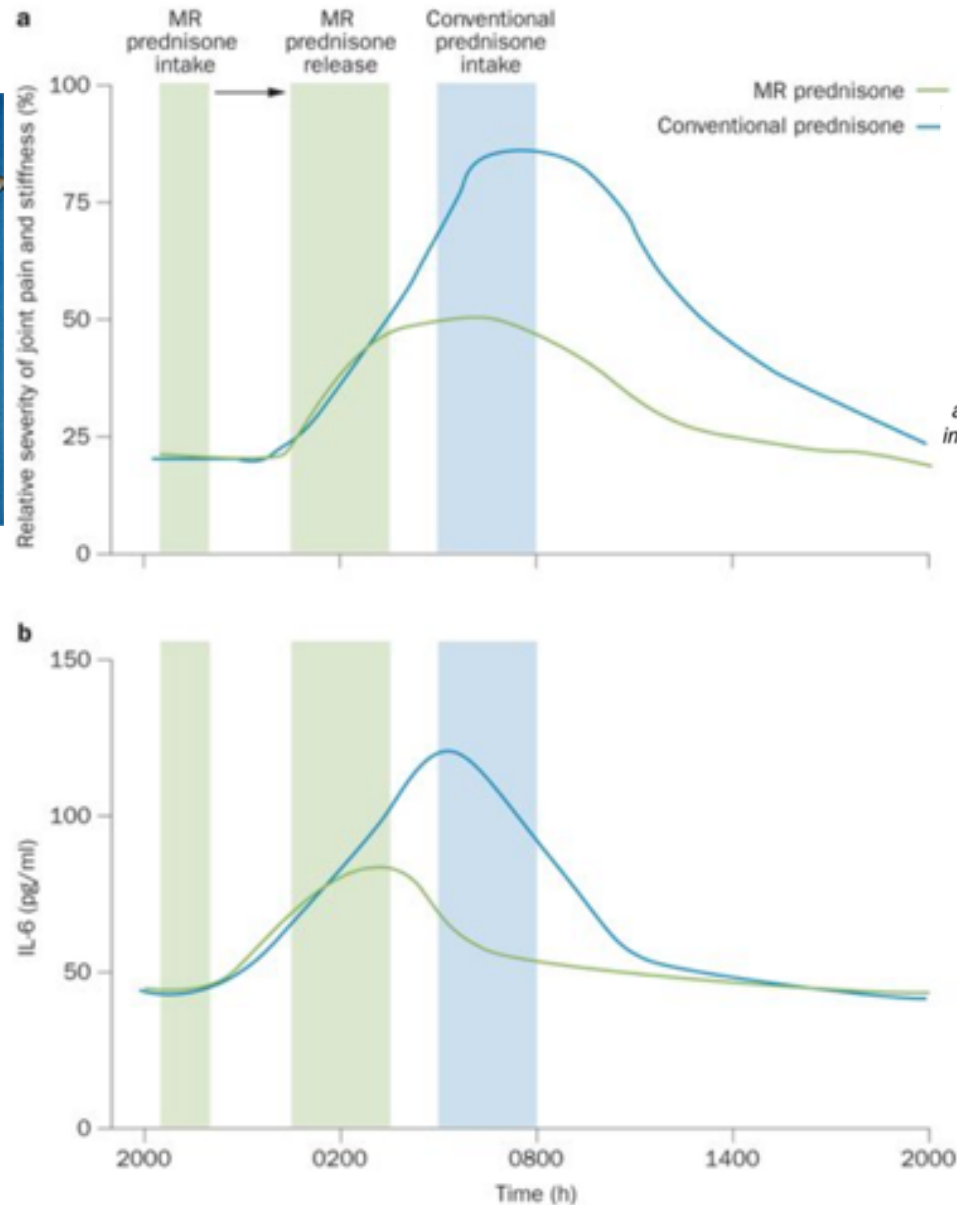


Chronotherapy workshop : relapsing RA patient mgmt

translate the 'circadian concept' in rheumatology from bench to bedside



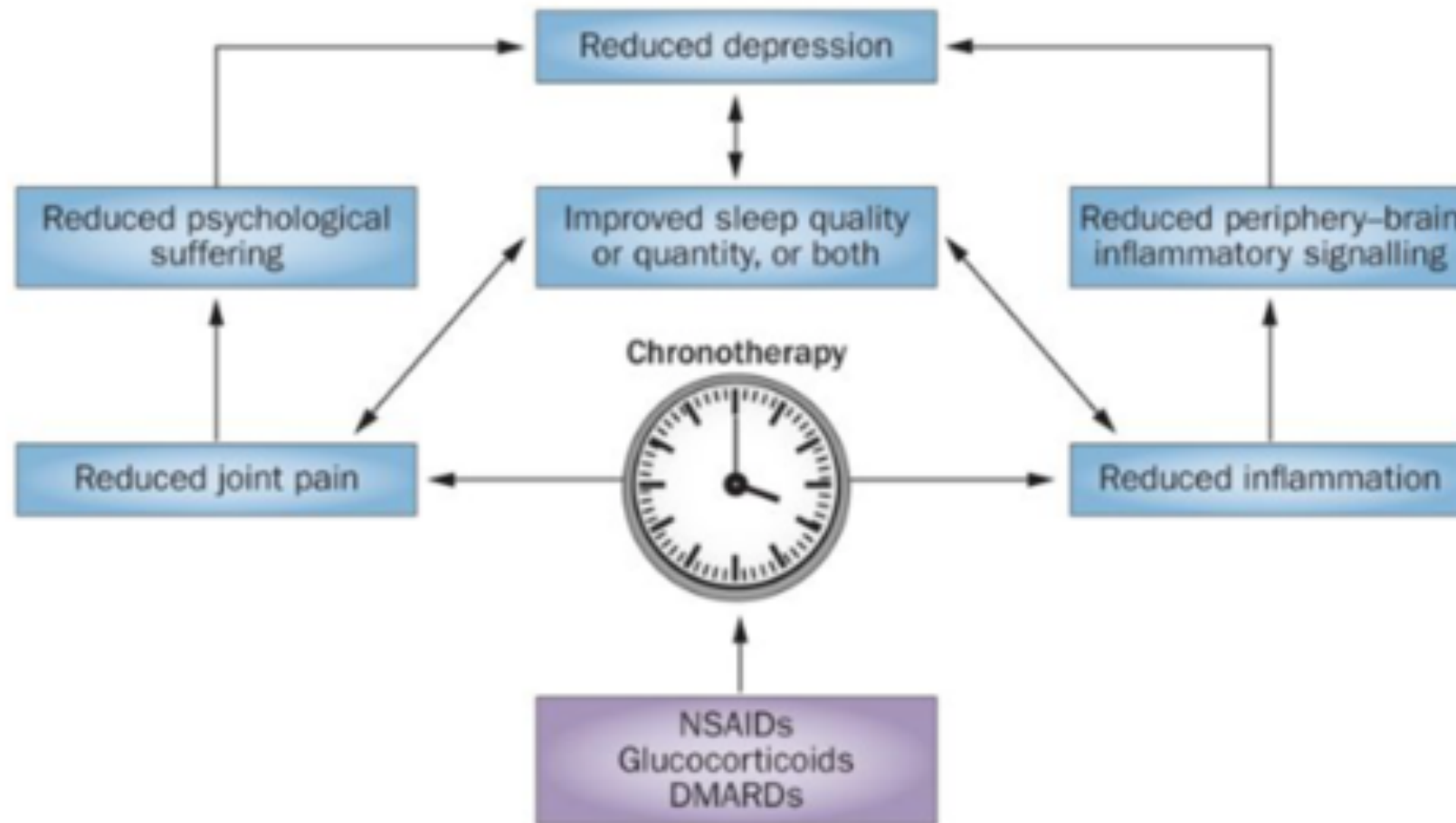
Figure 3: Responses to conventional prednisone versus chronotherapy for RA. MR : modified release



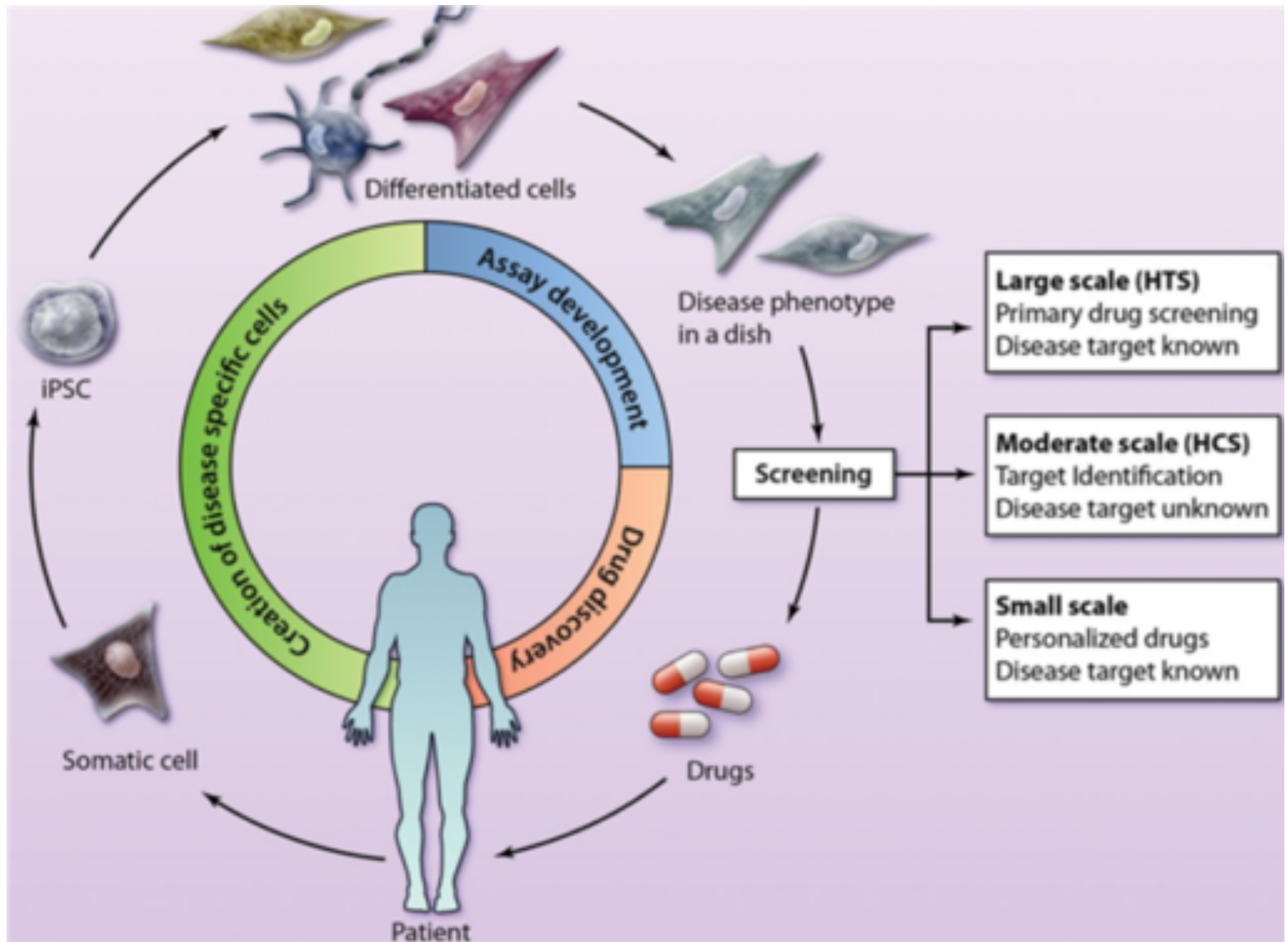
Buttgereit et al. 2012 Clinical and epidemiological research 72: 204-210



Figure 4: Effect of RA chronotherapy on associated depression.



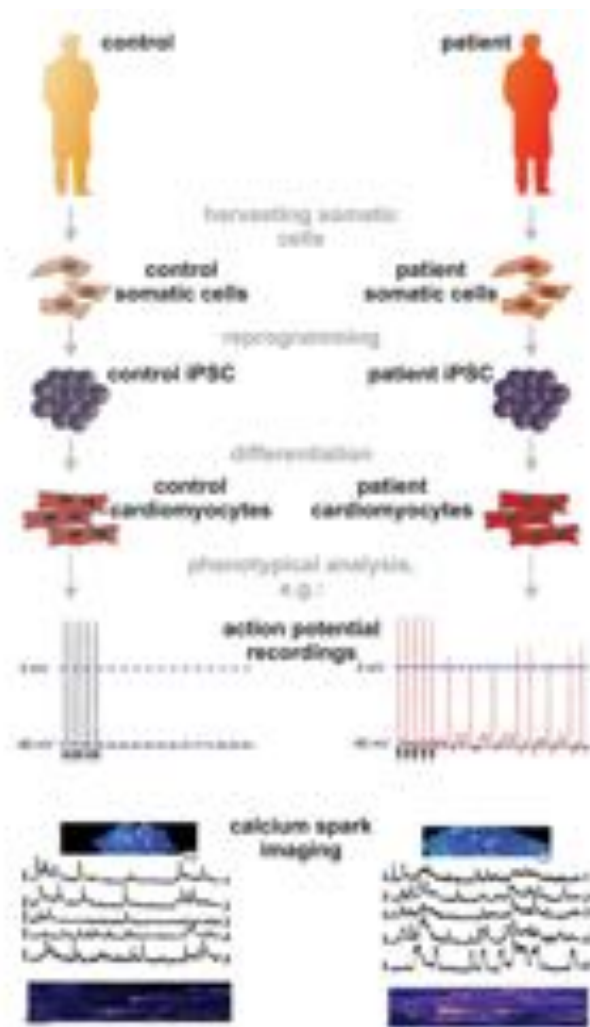
The Making Of An Innovative Medicine: iPSC in translational research



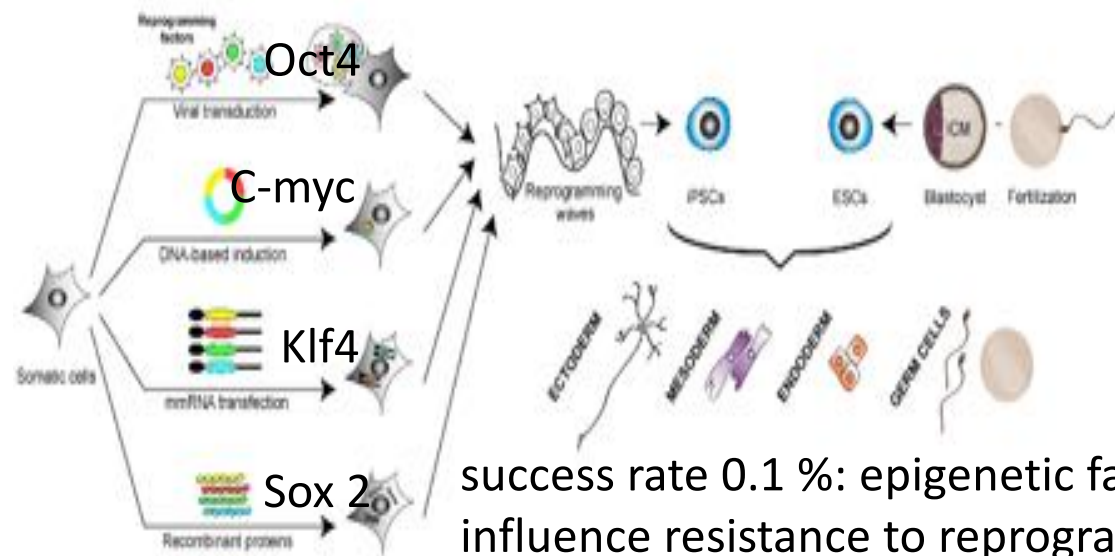
Session 3 : Translational Research : iPS closer to the patient



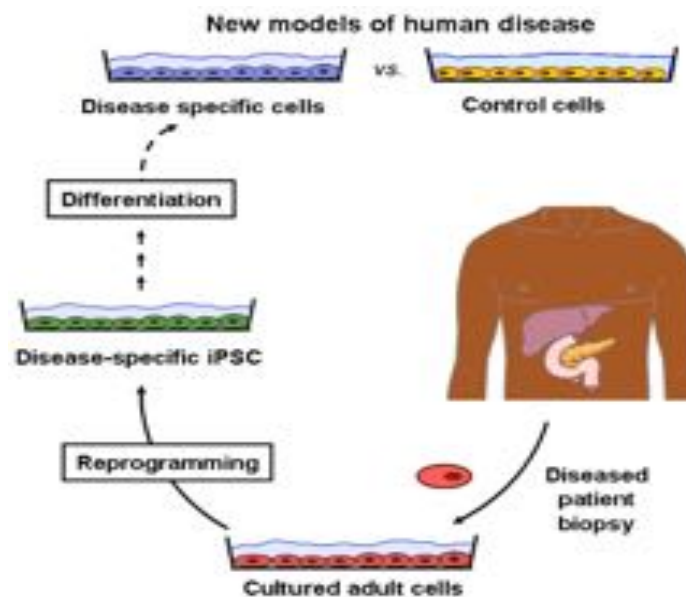
MODELING CARDIAC DISEASES WITH PATIENT SPECIFIC INDUCED PLURIPOTENTIAL STEM CELLS - iPS



Daniel Sinnecker et al. Circ Res. 2013;112:961-968



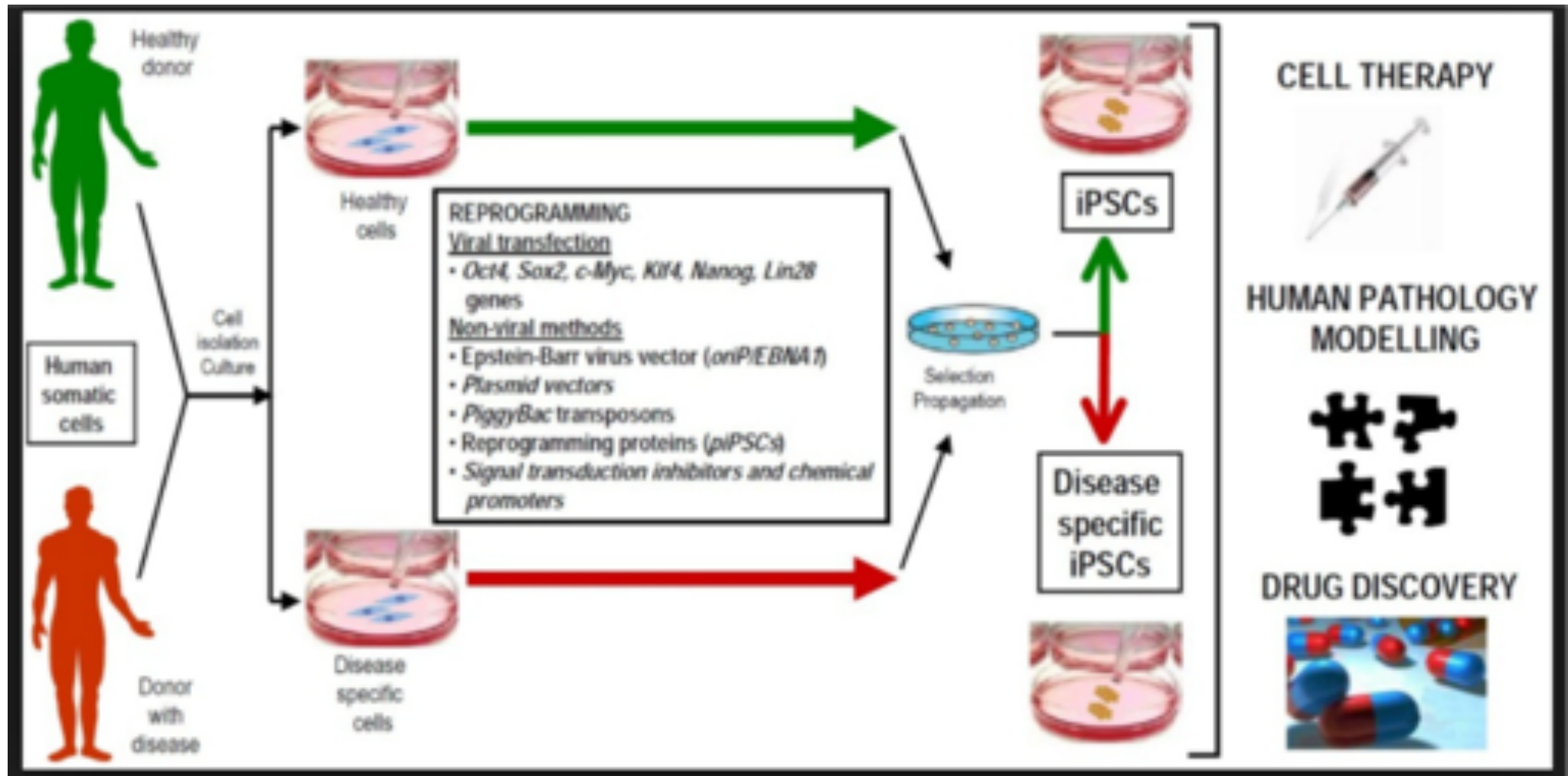
success rate 0.1 %: epigenetic factors influence resistance to reprogramming



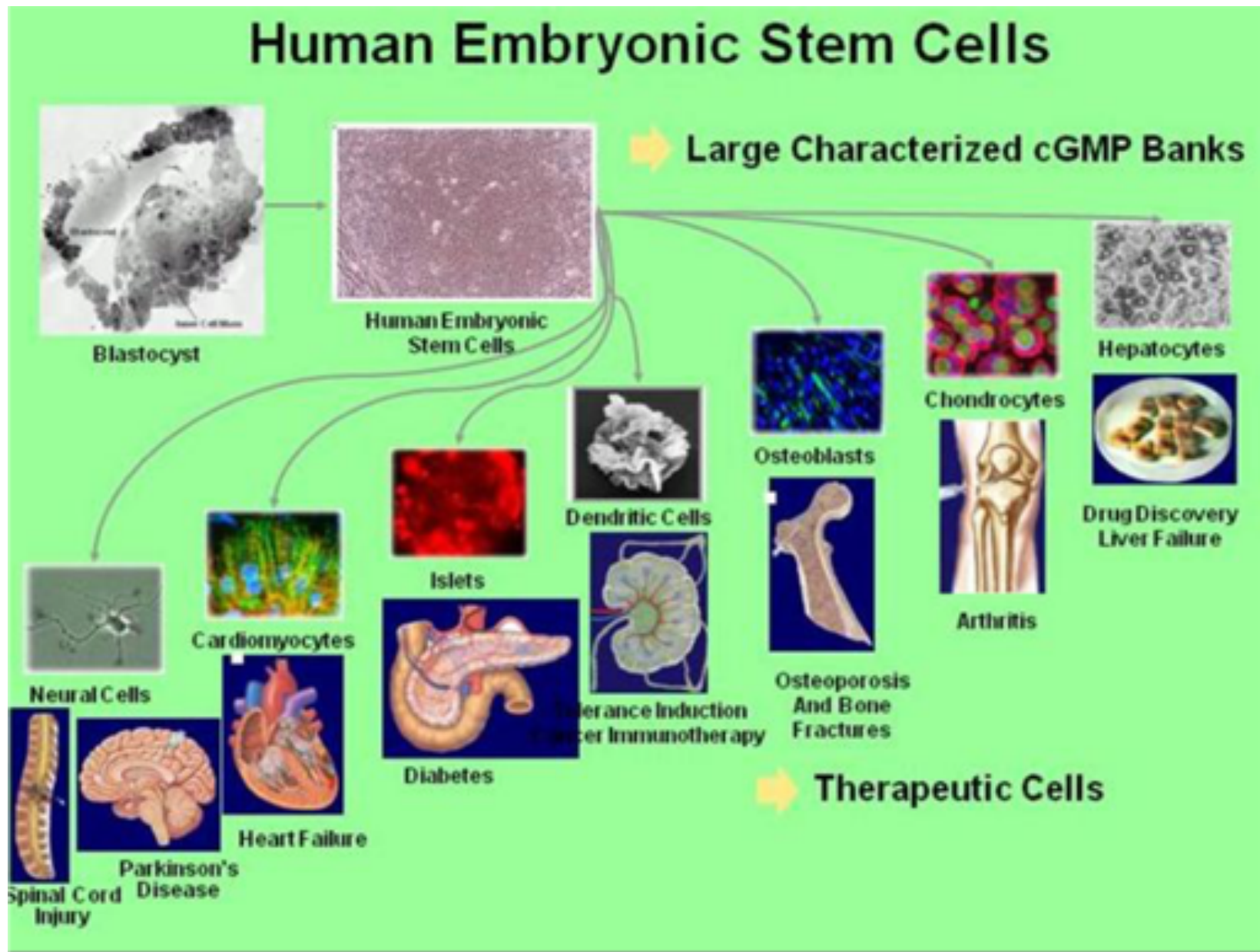
Shinya Yamanaka en 2013



MODELING DISEASES IN A DISH WITH PATIENT SPECIFIC INDUCED PLURIPOTENTIAL STEM CELLS - iPS



The Making Of An Innovative Medicine: iPSC



iPSC - the largest part of the
population suffer from incurable diseases



**People in the US affected by diseases that may be helped
by stem cell research**

Condition	Number of Persons Affected
Cardiovascular diseases	58 Million
Autoimmune diseases	30 Million
Diabetes	16 Million
Osteoporosis	10 Million
Cancer	8.2 Million
Alzheimer's disease	4 Million
Parkinson's disease	1.5 Million
Burns (severe)	0.3 Million
Spinal cord injuries	0.25 Million
Birth defects	150,000 (per year)
Total	128.4 Million

**PATIENTS SHALL BE AT
THE HEART OF WHAT WE
BIOMEDICAL SCIENTISTS
DO !**

**exemplary unmet
medical need:**

**Dementia-Alzheimer
2008 4 Millionen
cases**

**2025 10 Millionen
cases**

mit 60 J $p = 1/10^4$

Data from the Patients' Coalition for Urgent Research, Washington, DC (according to Perry, Ref. 267).

It is not because things are difficult that we do not dare, it is because we do not dare that they are difficult.

Lucius Annaeus Seneca



THANK YOU.....

DO YOU HAVE ANY QUESTIONS ?

HOW WAS YOUR SUMMER ?

