SAPIENZA
UNIVERSITÀ DI ROMA

SISTEMA SANITARIO REGIONALE
AZIENDA OSPEDALIERA UNIVERSITARIA
POLICLINICO UMBERTO I

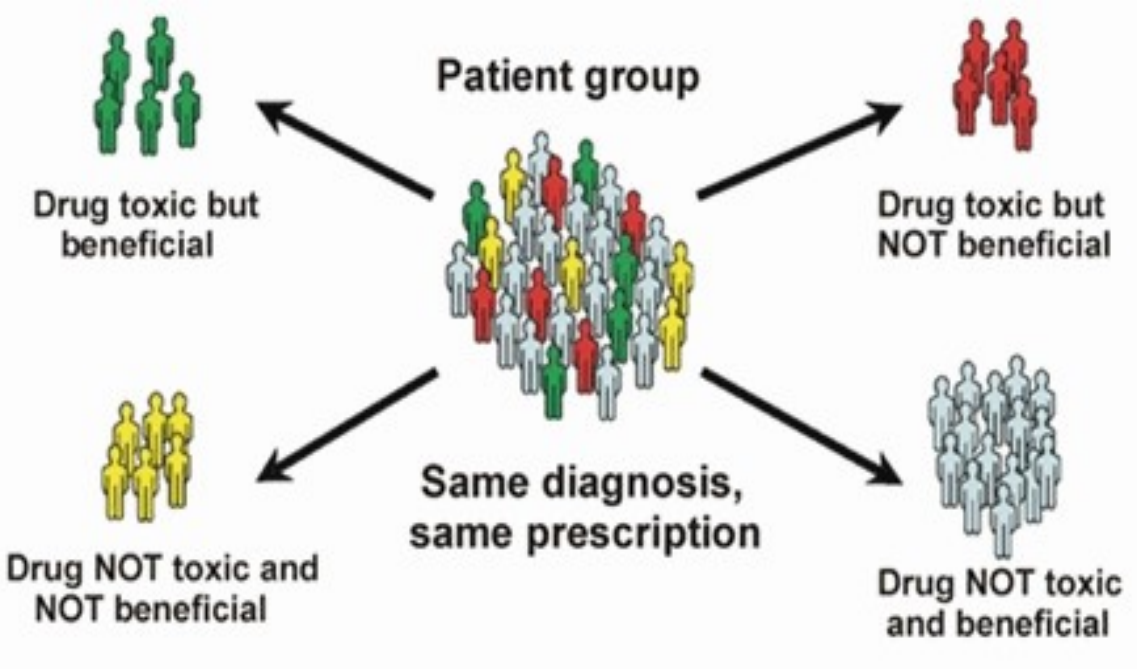
Medicina di precisione: realtà italiana oggi e aspettative future

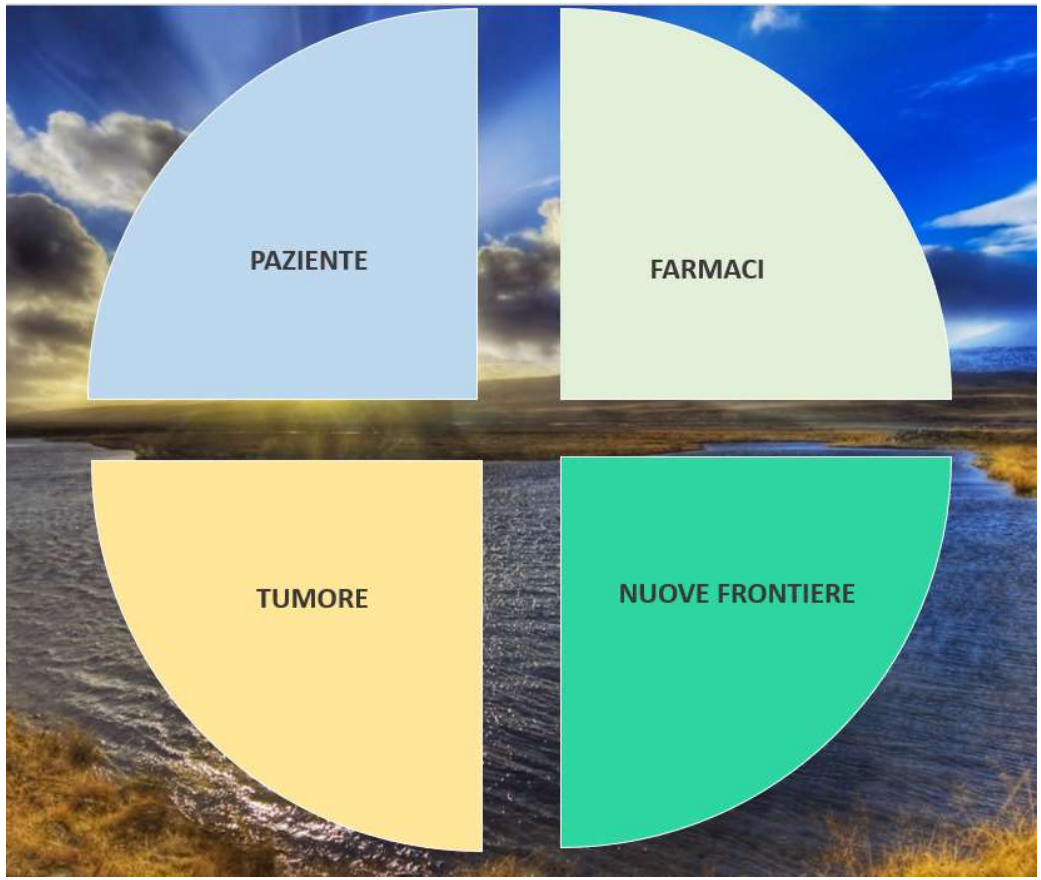
Andrea Botticelli
Policlinico Umberto I, Sapienza Università di Roma

PATIENT'S JOURNEY


FLORIDA
Miami
BAHAMAS
Nassau
OCEANO
ATLANTICO
GOLFO
DEL MESSICO
and Turk
PATIENT'S JOURNEY
REPUBBLICA
DOMINICANA
Cozumel
Grand Cayman
MESSICO
Ocho Rios
GIAMAICA
MAR DEI
CARAIBI
Roatan

VARIABILITÀ NELLA RISPOSTA AI FARMACI





IDENTIFICARE PAZ RESPONSIVI/RESISTENTI
IDENTIFICARE CHE SVILUPPERANNO TOSSICITÀ

PAZIENTE

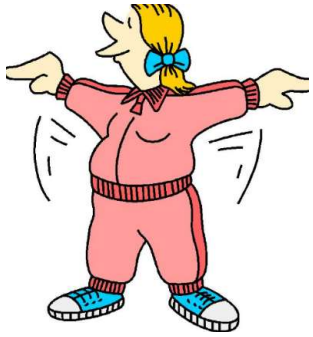
- **Età**
- **Comorbidità**
- **Stato funzionale**: performance status, scala di Karnofskj
- **•Funzionalità di organi vitali**
- **Stato sociale**
- **Composizione corporea**: massa grassa e massa magra

www.oncotarget.com Oncotarget, 2018, Vol. 9, (No. 39), pp: 25714-25722

Clinical Research Paper

Lean body mass wasting and toxicity in early breast cancer patients receiving anthracyclines

Federica Mazzuca[1,2], Concetta Elisa Onesti[1,3], Michela Roberto[1,2], Marco Di Girolamo[4], Andrea Botticelli[1], Paola Begini[5], Lidia Strigari[6], Paolo Marchetti[1,2] and Maurizio Muscaritoli[7]



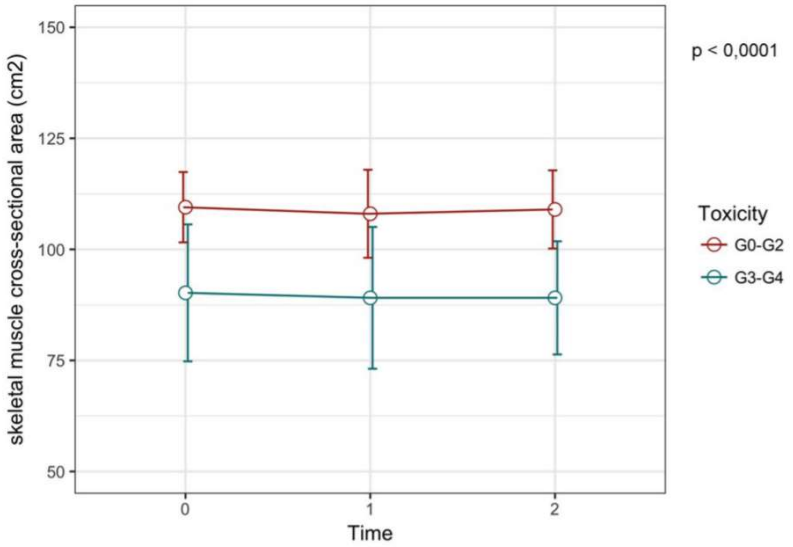
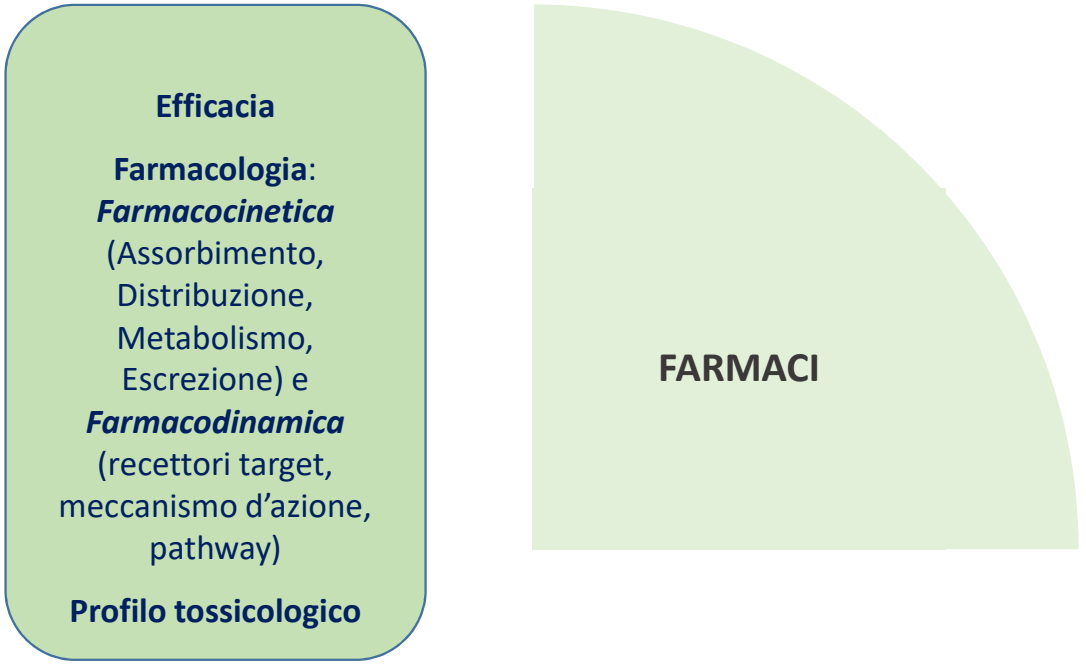
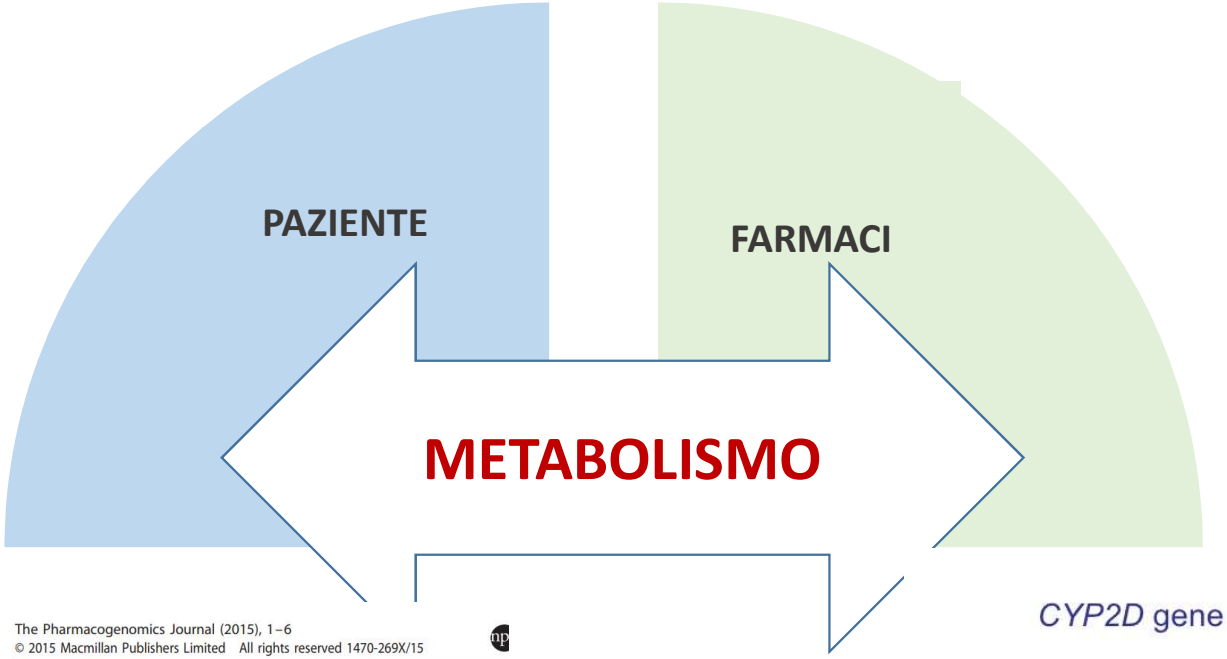


Figure 3: Skeletal muscle cross-sectional area variation according to toxicity grade. The red line show the skeletal muscle CSA at T0, T1 and T2 for the group of patients with G0-2 toxicities, while the blue line represent the variation of skeletal muscle CSA for


Efficacia
Farmacologia:
Farmacocinetica
(Assorbimento,
Distribuzione,
Metabolismo,
Escrezione) e
Farmacodinamica
(recettori target,
meccanismo d'azione,
pathway)
Profilo tossicologico
FARMACI


FLORIDA
BAHAMAS
Nassau
Miami
OCEANO
ATLANTICO
GOLFO
DEL MESSICO
FARMACO/PAZIENTE
Grand Turk
CUBA
REPUBBLICA
DOMINICANA
Cozumel
Grand Cayman
MESSICO
Ocho Rios
GIAMAICA
MAR DEI
CARAIBI
Roatan



The Pharmacogenomics Journal (2015), 1–6

www.nature.com/tpj

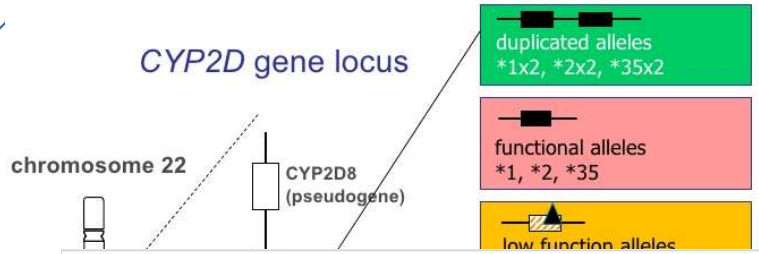
ORIGINAL ARTICLE

Genotype–phenotype correlations in 5-fluorouracil metabolism: a candid… prediction

G Gentile[1,2,5], A Botticelli[3,5], L Lionetto[2], F M…

Raccomandazioni 2019 per analisi farmacogenetiche

Ottobre 2019

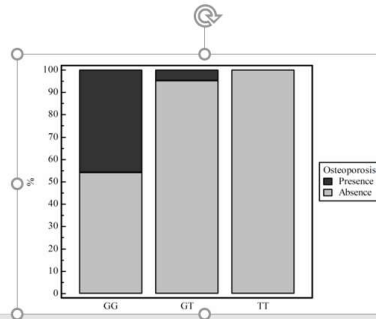


CYP19A1 Genetic Polymorphisms rs4646 and Osteoporosis in Patients Treated with Aromatase Inhibitor-Based Adjuvant Therapy

Table 2. Incidence of adverse effects, separately by CYP19A1 genotypes (n and %)

	CYP19A1 genotypes				
	Total sample n=45	GG (n=24; 53.3%)	GT (n=19; 42.2%)	TT (n=2; 4.4%)	p-value*
Fatigue	27 (60.0)	13 (54.2)	12 (63.2)	2 (100)	0.525
Pain	23 (51.1)	12 (50.0)	9 (47.4)	2 (100)	0.603
Hyper Cholesterolemia	20 (44.4)	11 (45.8)	8 (42.1)	1 (50.0)	1.000
Vaginal dryness	16 (35.6)	11 (45.8)	4 (21.1)	1 (50.0)	0.190
Nausea & vomiting	13 (28.9)	6 (25.0)	5 (26.3)	2 (100)	0.118
Osteoporosis	11 (24.4)	11 (45.8)	0 (0.0)	0 (0.0)	0.001
Sleep disturbances	11 (24.4)	7 (29.2)	2 (10.5)	2 (100)	0.031
Cephalea	5 (11.1)	1 (4.2)	4 (21.1)	0 (0.0)	0.255
Cutaneous rash	5 (11.1)	3 (12.5)	2 (10.5)	0 (0.0)	1.000
Diarrhoea	5 (11.1)	2 (8.3)	2 (10.5)	1 (50.0)	0.333
Anorexia	5 (11.1)	2 (8.3)	3 (15.8)	0 (0.0)	0.717
Hyper Triglygeridemia	4 (8.9)	2 (8.3)	2 (10.5)	0 (0.0)	1.000
Dysthyroidism	4 (8.9)	4 (16.7)	0 (0.0)	0 (0.0)	0.269

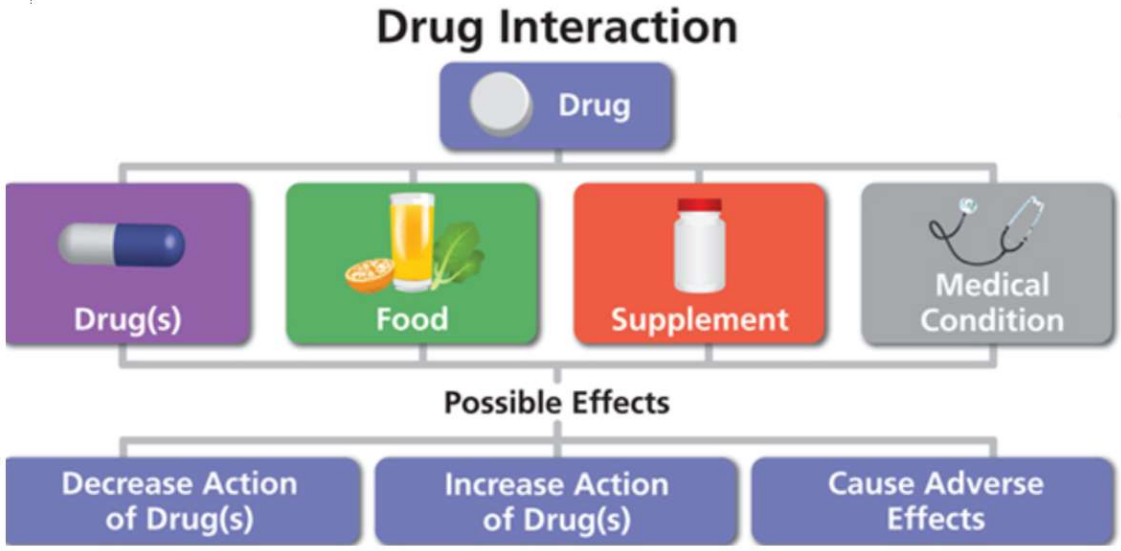
*Chi squared, Fisher's exact test
Hyper Cholesterolemia (>200 mg/dL); Hyper Triglygeridemia (>150 mg/dL)



PAZIENTE

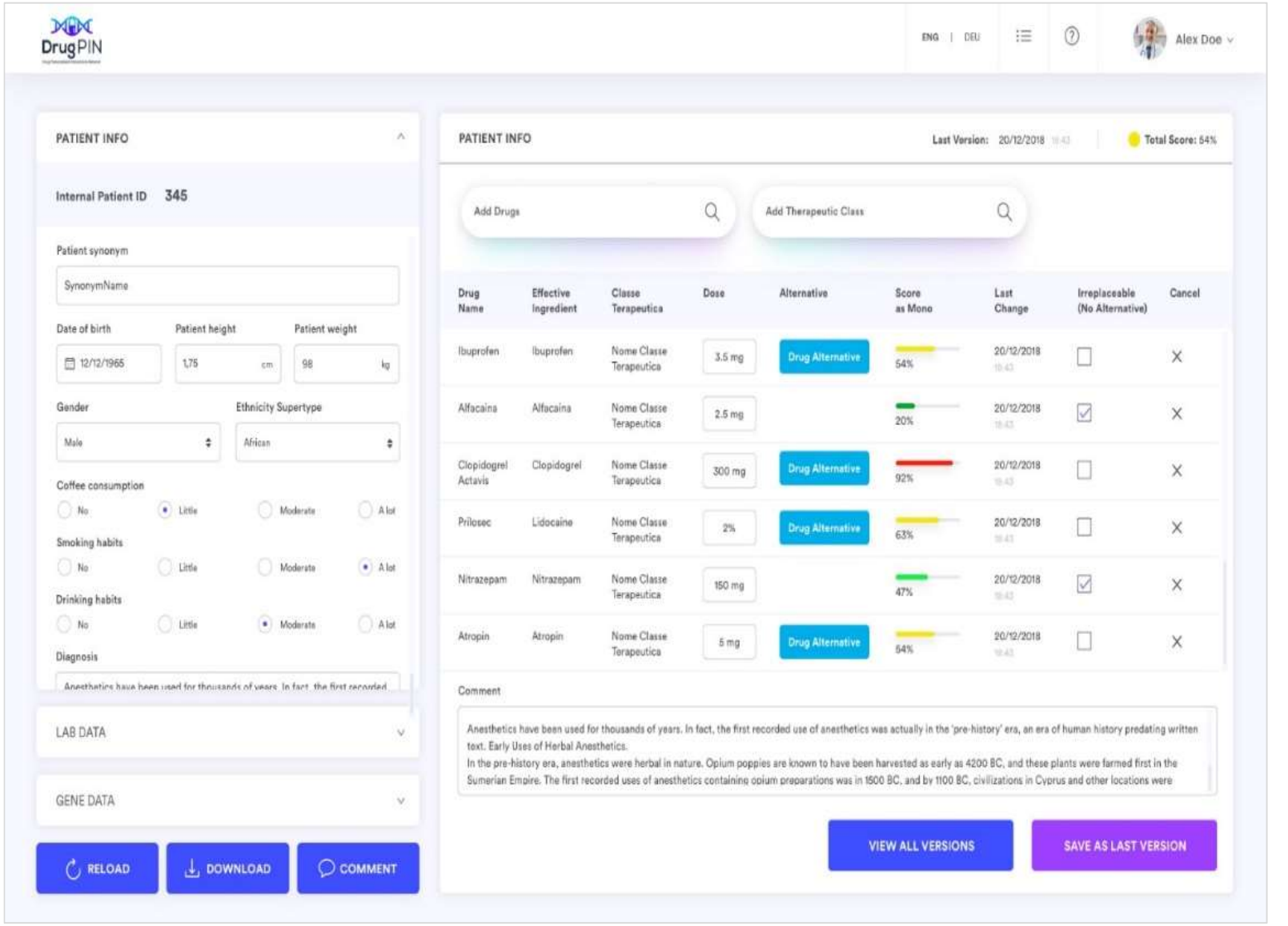
FARMACI

INTERAZIONE DEI FARMACI



COMORBIDITÀ E POLIFARMACOTERAPIA

- 2/3 degli anziani >65aa assume 1 o più farmaci al giorno
- Gli anziani >70 aa assumono 3 o più farmaci al giorno
- Gli anziani istituzionalizzati assumono da 4 a 8 farmaci al giorno


DrugPIN
ENG | DEU
Alex Doe
PATIENT INFO
Internal Patient ID 345
Patient synonym
SynonymName
Date of birth
12/12/1965
Patient height
1,75 cm
Patient weight
98 kg
Gender
Male
Ethnicity Supertype
African
Coffee consumption
No
Little
Moderate
A lot
Smoking habits
No
Little
Moderate
A lot
Drinking habits
No
Little
Moderate
A lot
Diagnosis
Anesthetics have been used for thousands of years. In fact, the first recorded
LAB DATA
GENE DATA
RELOAD
DOWNLOAD
COMMENT
PATIENT INFO
Last Version: 20/12/2018
Total Score: 54%
Add Drugs
Add Therapeutic Class
Drug Name
Effective Ingredient
Classe Terapeutica
Dose
Alternative
Score as Mono
Last Change
Irreplaceable (No Alternative)
Cancel
Ibuprofen
Ibuprofen
Nome Classe Terapeutica
3.5 mg
Drug Alternative
54%
20/12/2018
Alfacaina
Alfacaina
Nome Classe Terapeutica
2.5 mg
20%
20/12/2018
Clopidogrel Actavis
Clopidogrel
Nome Classe Terapeutica
300 mg
Drug Alternative
92%
20/12/2018
Prilosec
Lidocaine
Nome Classe Terapeutica
2%
Drug Alternative
63%
20/12/2018
Nitrazepam
Nitrazepam
Nome Classe Terapeutica
150 mg
47%
20/12/2018
Atropin
Atropin
Nome Classe Terapeutica
5 mg
Drug Alternative
54%
20/12/2018
Comment
Anesthetics have been used for thousands of years. In fact, the first recorded use of anesthetics was actually in the 'pre-history' era, an era of human history predating written text. Early Uses of Herbal Anesthetics.
In the pre-history era, anesthetics were herbal in nature. Opium poppies are known to have been harvested as early as 4200 BC, and these plants were farmed first in the Sumerian Empire. The first recorded uses of anesthetics containing opium preparations was in 1500 BC, and by 1100 BC, civilizations in Cyprus and other locations were
VIEW ALL VERSIONS
SAVE AS LAST VERSION

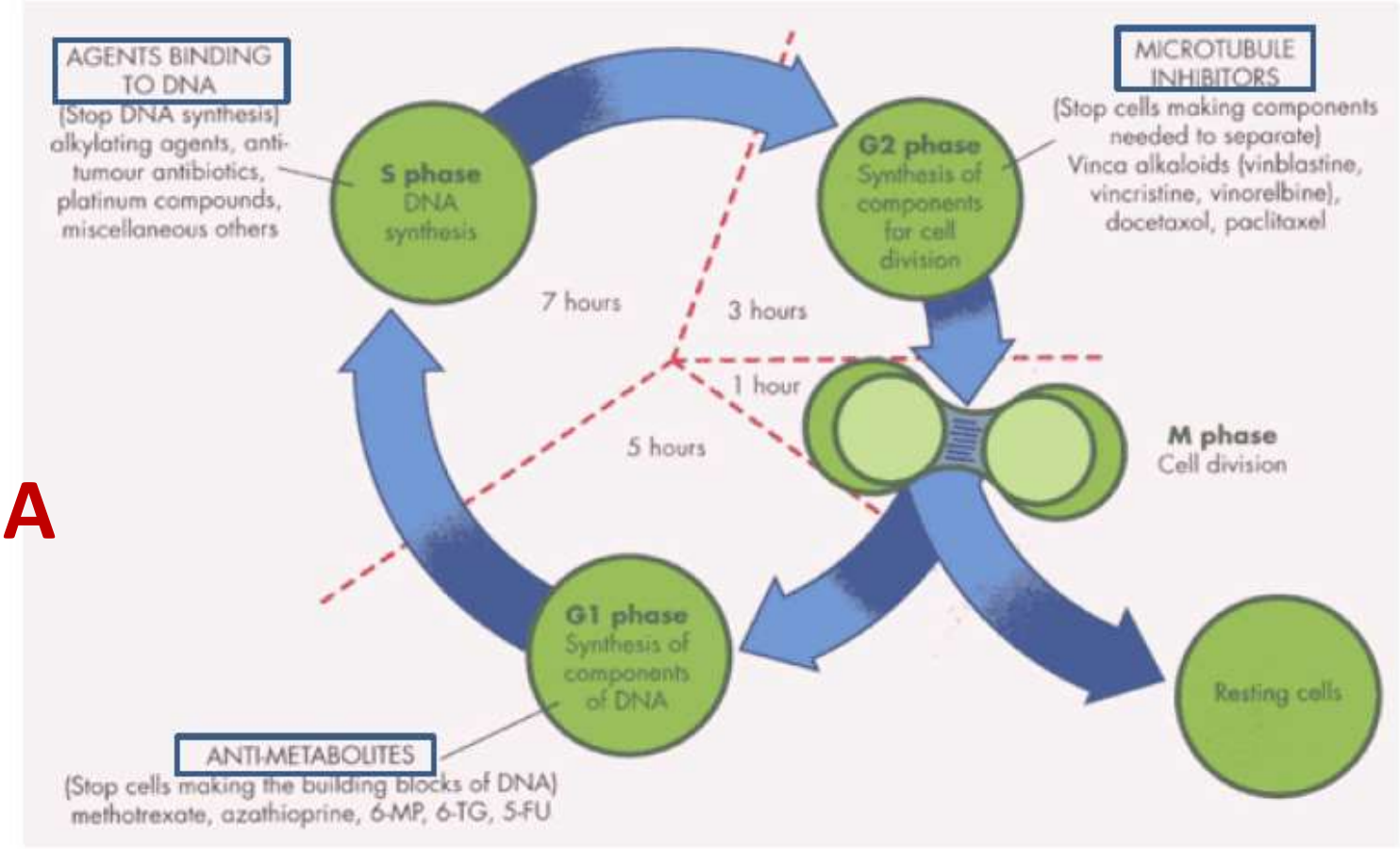
CA

Presentazione del progetto di ricerca:
Carta d'identità del Paziente


FLORIDA
BAHAMAS
Nassau
Miami
OCEANO
ATLANTICO
GOLFO
DEL MESSICO
FARMACO/PAZIENTE
Gra
MONDO DEL PROFILO
GENOMICO
CUBA
REPUBBLICA
DOMINICANA
Cozumel
Grand Cayman
MESSICO
Ocho Rios
GIAMAICA
MAR DEI
CARAIBI
Roatan

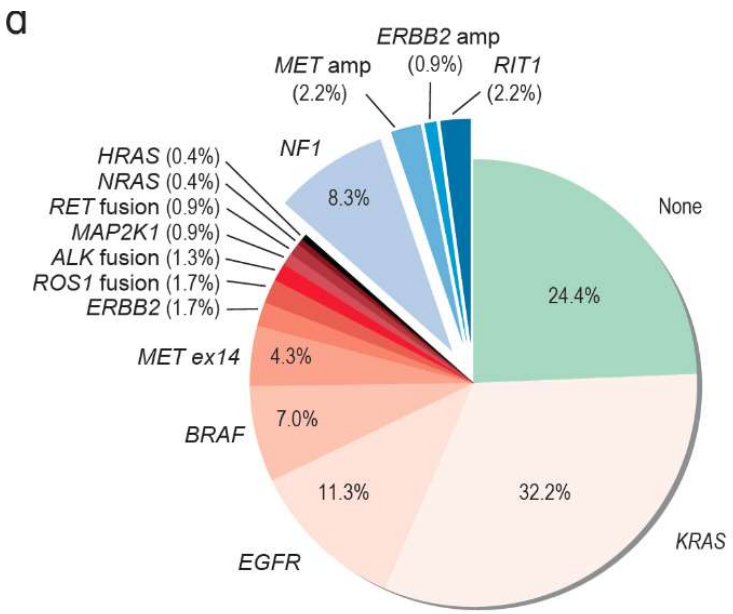
AGISCE SUL CICLO CELLULARE

SIAMO PARTITI CON LA CHEMIOTERAPIA

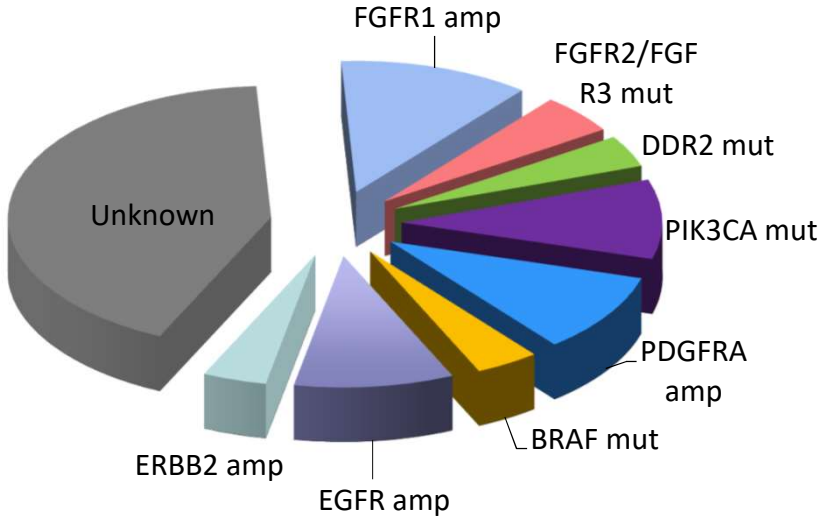


But are they able to discriminate between cancer cells and normal cells?

DOBBIAMO CONOSCERE LE MUTAZIONI…



Adenocarcinoma



Squamous Cell carcinoma

PROFILAZIONE MOLECOLARE

FOUNDATIONONE® LIQUID CDx

PATIENT
03-2021-00033917, IT

REPORT DATE
27 Jan 2021
ORDERED TEST #
ORD-0997078-01

ABOUT THE TEST FoundationOne®Liquid CDx is a next generation sequencing (NGS) assay that identifies clinically relevant genomic alterations in circulating cell-free DNA.

PATIENT

a

MEDICAL FACILITY ID 320941
PATHOLOGIST Not Provided

SPECIMEN

SPECIMEN ID 6 1/1/1958
SPECIMEN TYPE Blood
DATE OF COLLECTION 15 January 2021
SPECIMEN RECEIVED 18 January 2021

Genomic Signatures

Microsatellite status - MSI-High
Blood Tumor Mutational Burden - 37 Muts/Mb
Tumor Fraction - Cannot Be Determined

Gene Alterations

For a complete list of the genes assayed, please refer to the Appendix.

BRCA2 N2556fs*10
ERBB2 V842I
FBXW7 R278*
PIK3CA R88Q
PTEN K267fs*9
ARID1A P225fs*175, D1850fs*33
KRAS G13D
RNF43 G659fs*41, R113*
SUFU P24fs*72
CDH1 A634V
CDKN2A/B p16INK4a splice site 151-1G>T and p14ARF splice site 194-1G>T, p16INK4a R80* and p14ARF P94L
FGF23 R176Q
MAP3K13 R478W
MLL2 P2354fs*30
MSH6 E1272fs*3
QKI K134fs*14
SETD2 R2094fs*53
SRC E527K
TGFBR2 K128fs*3
TP53 R273C

19 Therapies Approved in the EU
0 Therapies with Lack of Response
58 Clinical Trials

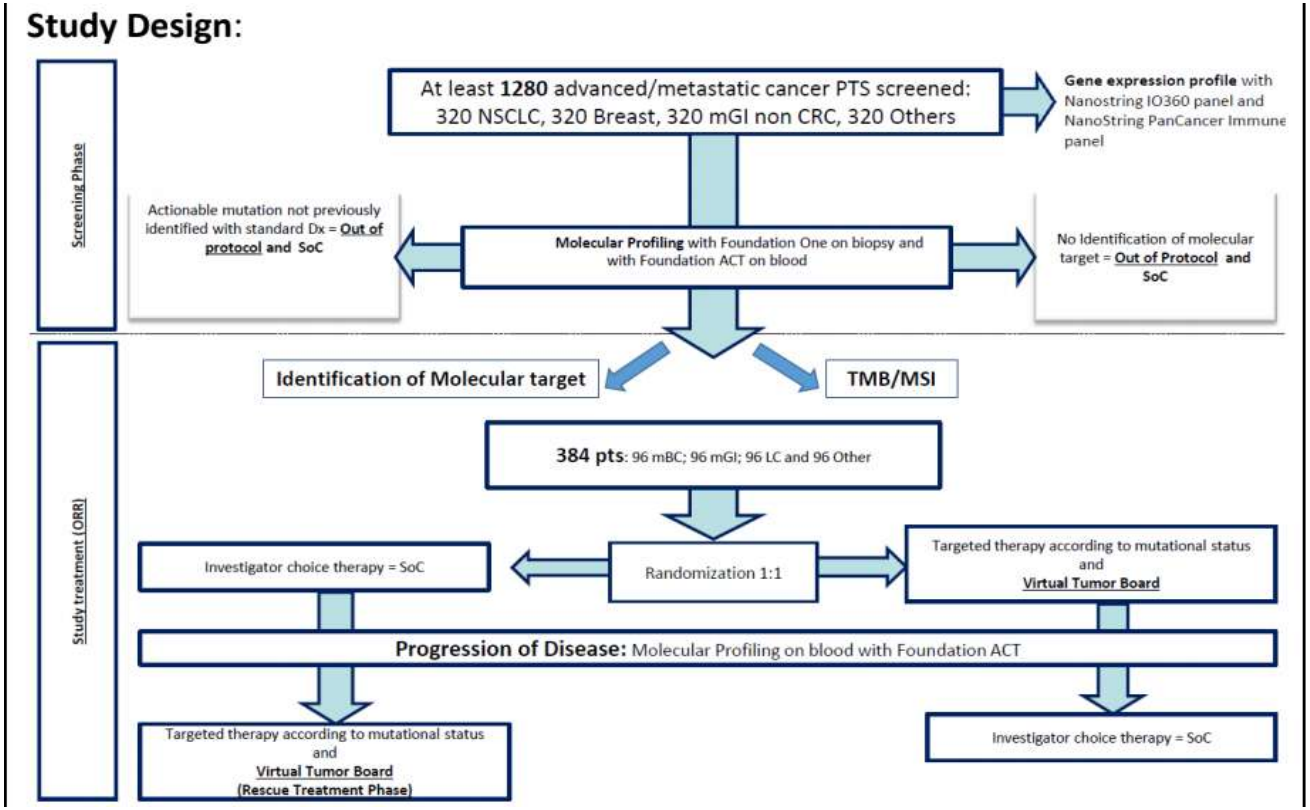
Molecular Tumor Board

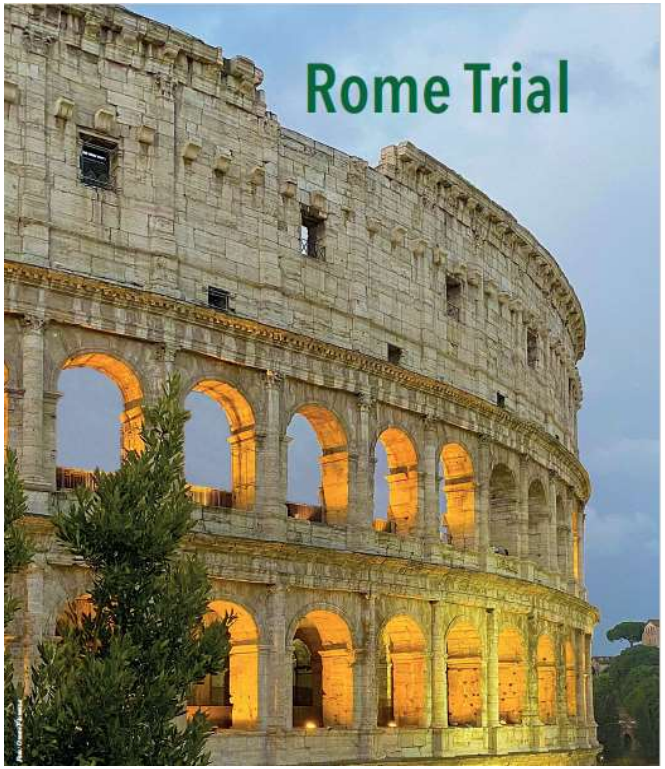
From a standard pre-defined therapy
to a personalized treatment

ONCOLOGO, BIOLOGO MOLECOLARE, IMMUNOLOGO, ANATOMOPATOLOGO, GENETISTA, FARMACOLOGO…

The ROME trial from histology to target: the road to personalize target therapy and immunotherapy

Study Design:





41 CENTERS IN ITALY

ONCOTYPE DX :

DOPO L'INTERVENTO CHIRURGICO

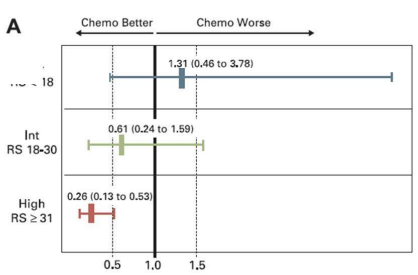
QUALE è IL RISCHIO CHE TORNI LA MALATTIA ?

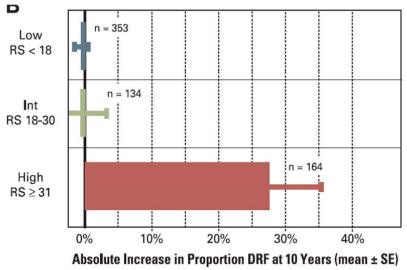
CHEMIO O NON CHEMIO ?

Oncotype DX® in Node Negative BC

Paik , JCO 2006

- NSABP B-20 :ER+, N0, CT (CMF regimen); 651pts (227 TAM /424 TAM+CT)
- **High RS (≥ 31): benefited from CT** (RR 0.26 (95% CI, 0.13 -0.53), relative risk reduction in 10 yrs **27.6%** (SE 8.0%))
- **Low RS (< 18) no significant benefit from CT** (RR 1.31 (95% CI, 0.46 – 3.78), relative risk reduction in 10 yrs **-1.1%** (SE 2.2%))



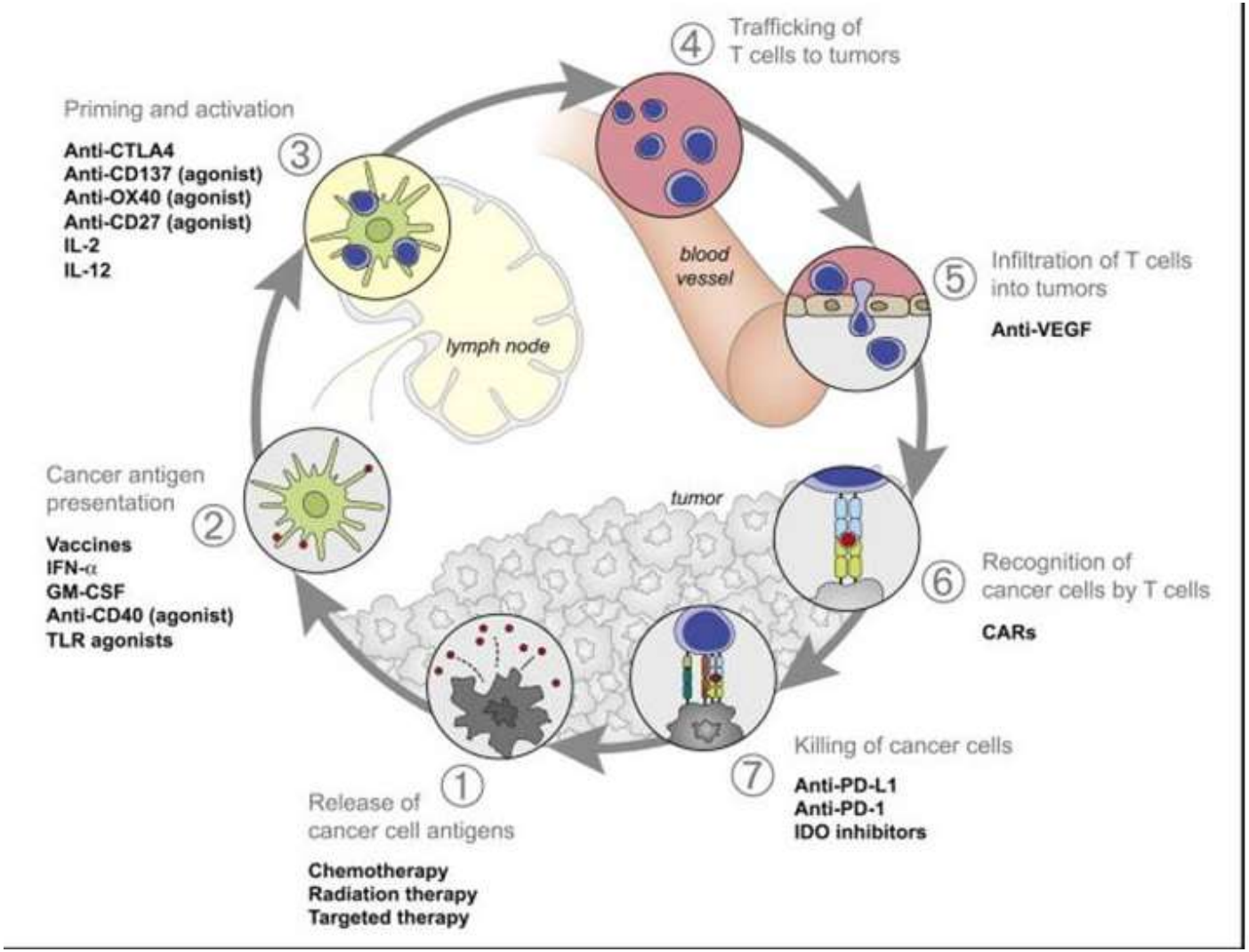


Cardoso at 2016 ASCO


FLORIDA
BAHAMAS
Nassau
Miami
OCEANO
ATLANTICO
GOLFO
DEL MESSICO
FARMACO/PAZIENTE
MONDO DEL PROFILO
GENOMICO
CUBA
REPUBBLICA
DOMINICANA
Cozumel
IMMUNOTERAPIA
MESSICO
MAR DEI
CARAIBI
Roatan

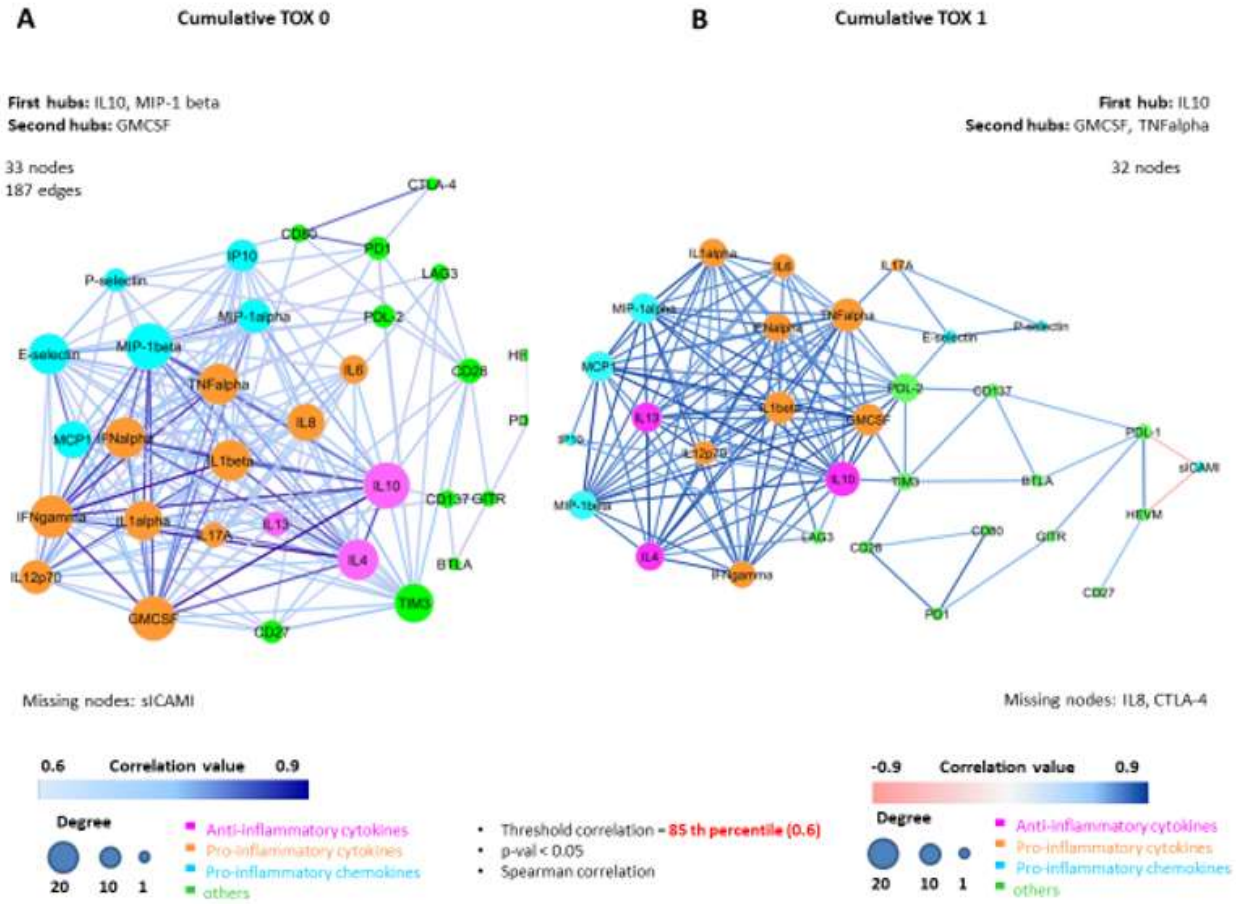

IMMUNOTHERAPY:
Using the Body To Fight Cancer

CICLO CANCRO-IMMUNITà

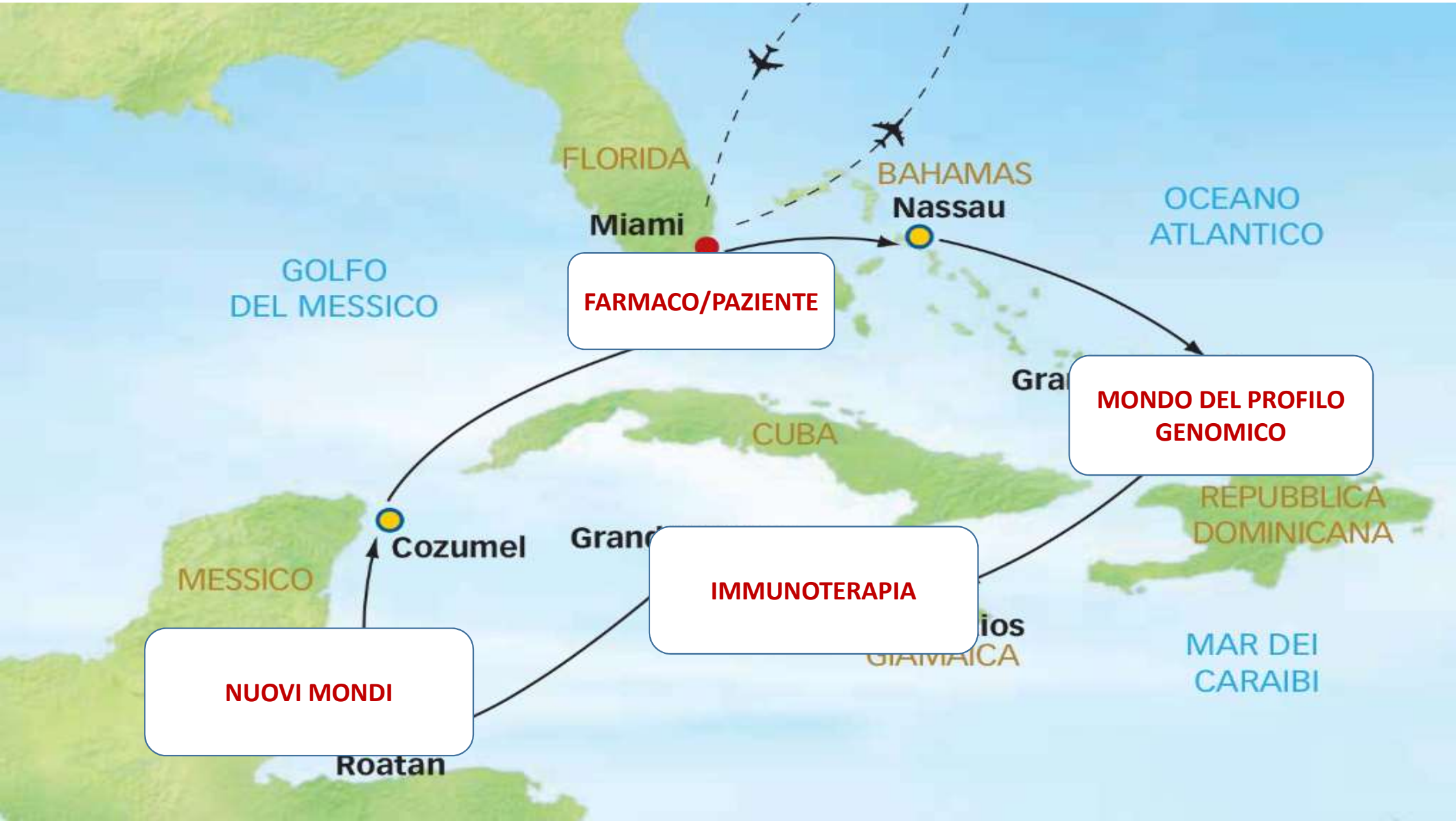


NON TUTTI I PAZIENTI RISPONDONO !!!!

CARTA DI IDENTITÀ IMMUNOLOGICA

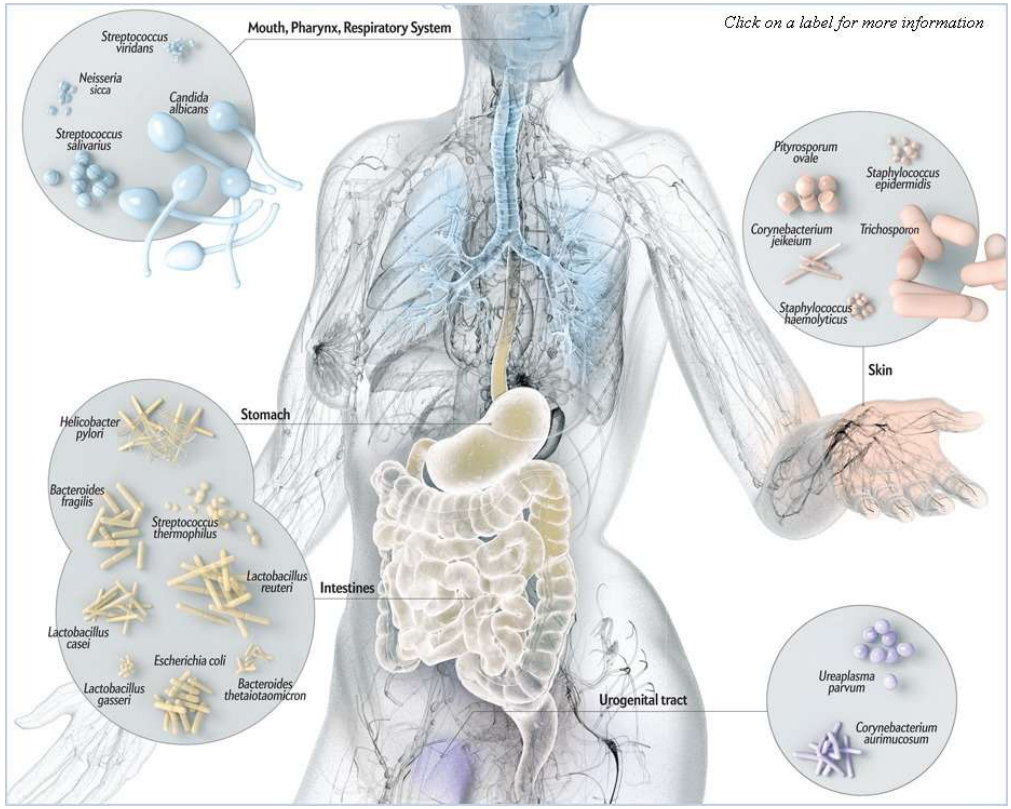


Botticelli, Zizzari,Nuti, Marchetti. FRONTIERS IN IMMUNOLOGY


FLORIDA
Miami
BAHAMAS
Nassau
OCEANO ATLANTICO
GOLFO DEL MESSICO
FARMACO/PAZIENTE
Gra
MONDO DEL PROFILO GENOMICO
CUBA
REPUBBLICA DOMINICANA
Cozumel
Grand
MESSICO
IMMUNOTERAPIA
ios
GIAMAICA
MAR DEI CARAIBI
NUOVI MONDI
Roatan

MICROBIOTA

CHI è IL MICROBIOTA ?



BATTERI E ALTRI MICROORGANISMI (fungi, protozoa, viruses)

NEL CORPO SONO STIMATI **10 VOLTE** Più BATTERI CHE CELLULE UMANE (10^{14})

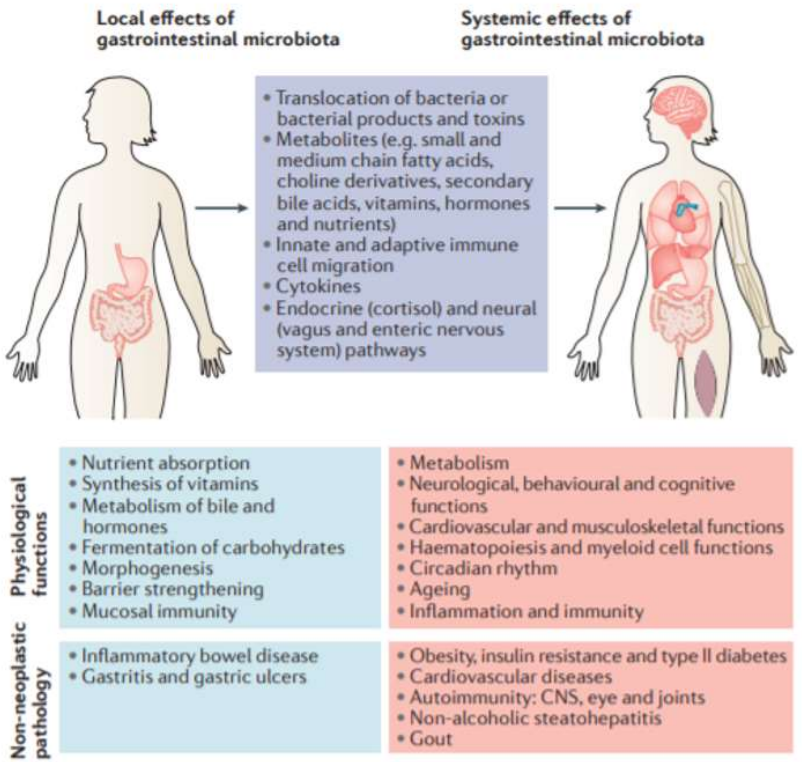
300-500 SPECIE (main phyla: Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria)

MUTUALISMO DEL MICROBIOTA

detta anche simbiosi mutualistica, che comporta un **VANTAGGIO RECIPROCO** per gli individui associati

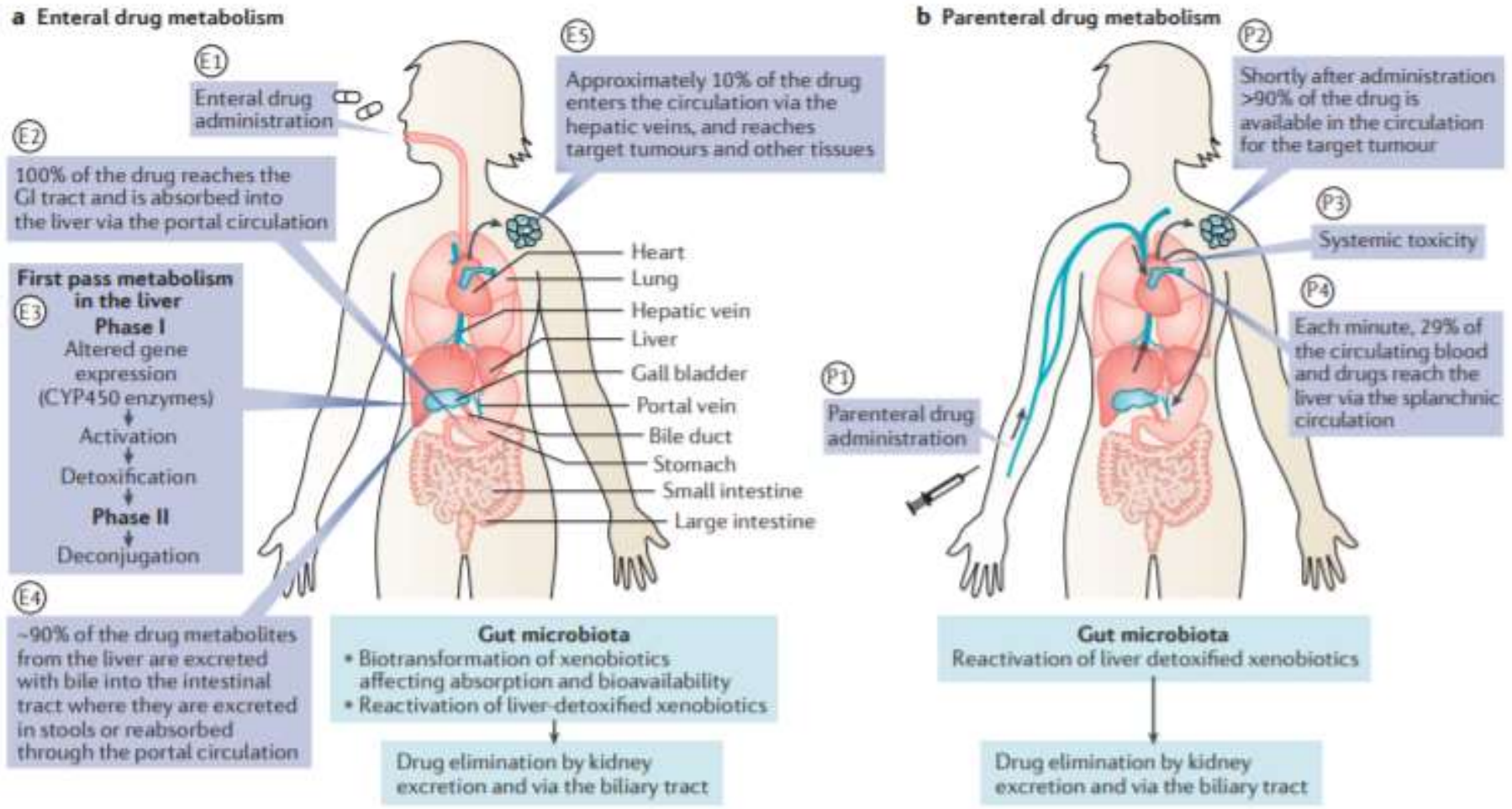
il microbiota intestinale interagendo con cellule intestinali epiteliali e stromali :

- ✓ regola le funzioni di barriera,
- ✓ modula l'immunità,
- ✓l'omeostasi immunitaria delle mucose,
- ✓previene l'infestazione da parte di agenti patogeni,
- ✓Trasforma le fibre alimentari,
- ✓sintetizza le vitamine,
- ✓ metabolizza gli ormoni
- ✓promuove l'ematopoiesi del midollo osseo



Roy, 2017

IL MICROBIOTA METABOLIZZA FARMACI



Roy, 2017

POSSIAMO MODULARLO

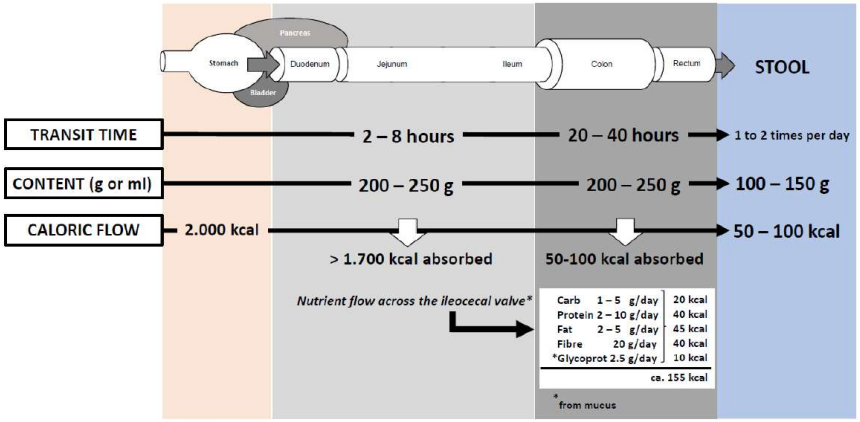


Fig 2: Selected gastrointestinal functions and parameters known to affect stool sample mass and composition as well as substrate flow across the ileoceacal valve for metabolic use by the microbiota (for details see text).

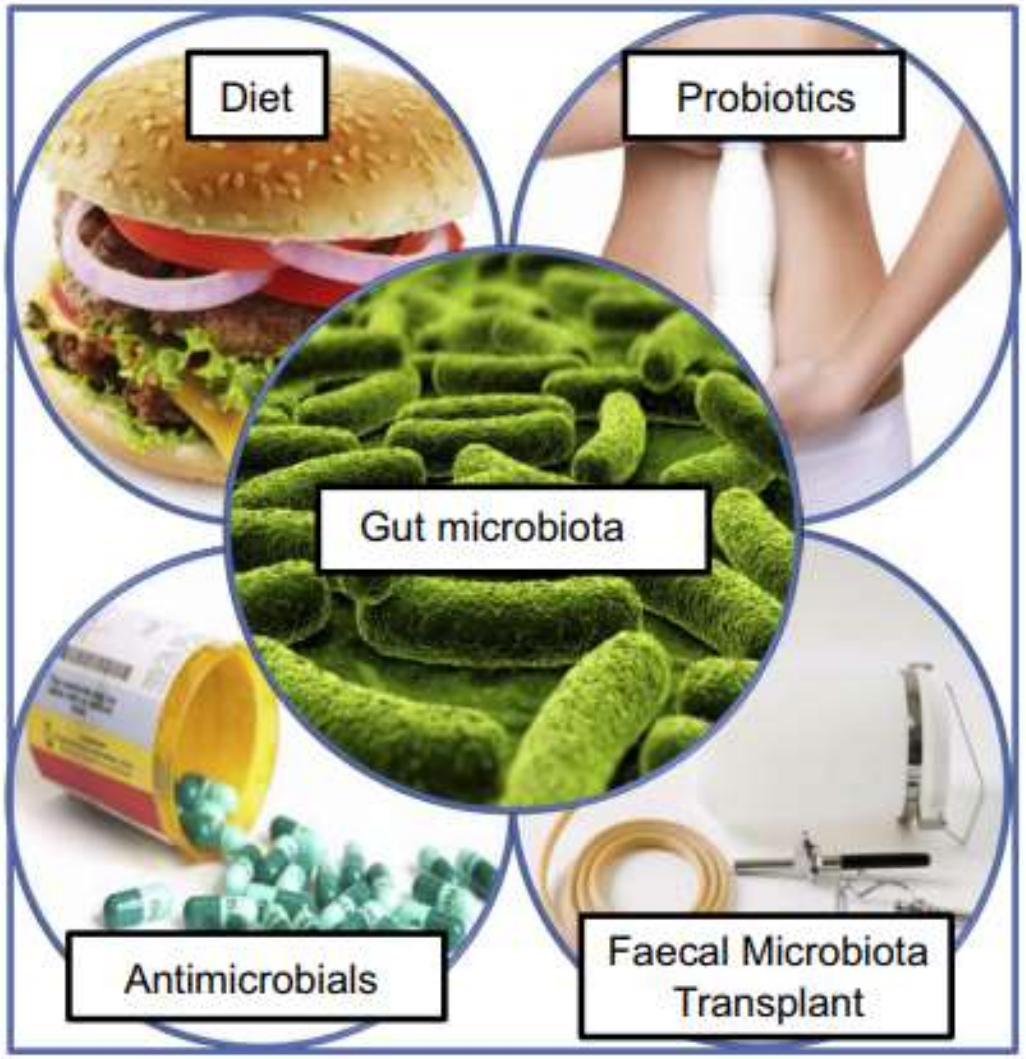
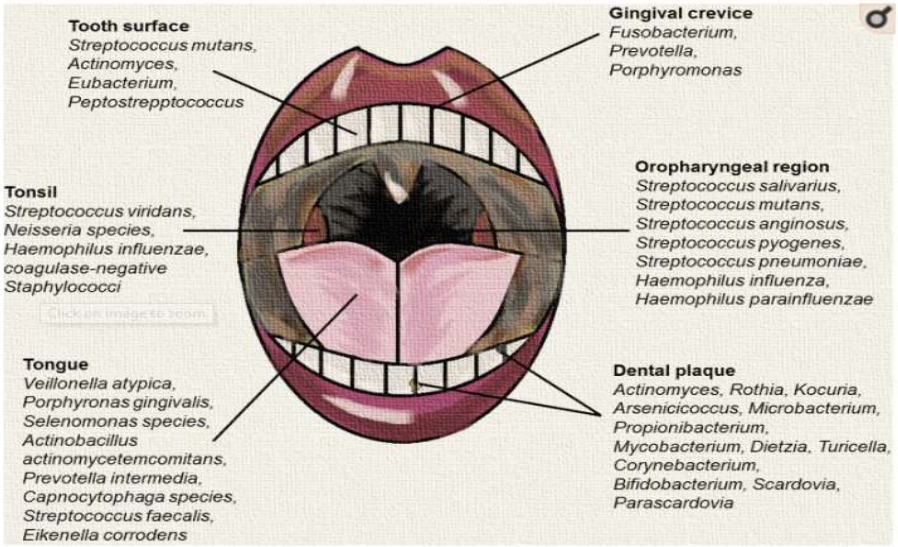


Fig. 1. Potential strategies for manipulation of the gut microbiota.

IL MICROBIOTA SI ASSOCIA A TIPI DIVERSI DI NEOPLASIA

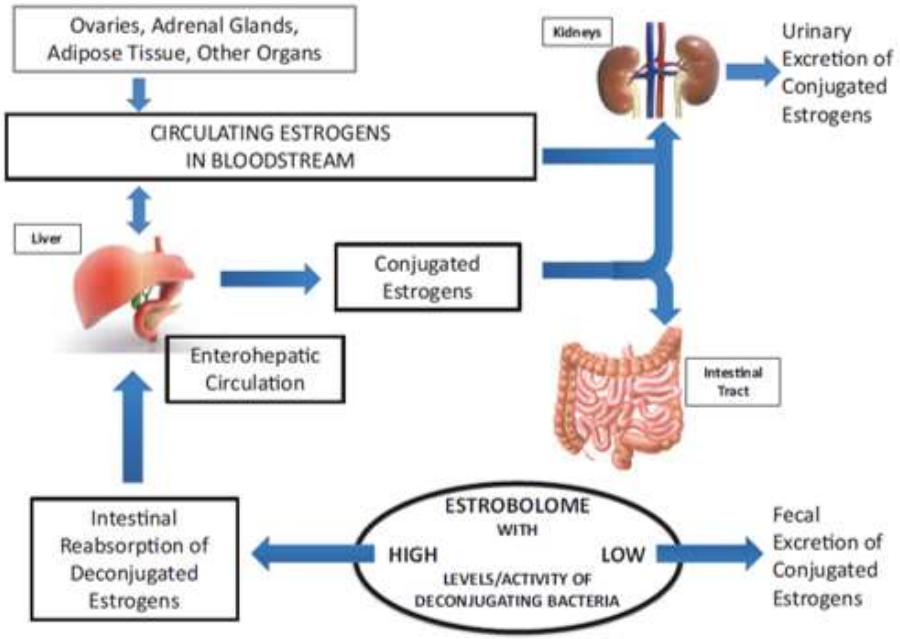
Mini-Review

Gut Microbiota and Colorectal Cancer



The Intestinal Microbiome and Estrogen Receptor–Positive Female Breast Cancer

Maryann Kwa, Claudia S. Plottel, Martin J. Blaser, Sylvia Adams



From Breast Cancer to Antimicrobial:
Combating Extremely Resistant Gram-Negative
"Superbugs" Using Novel Combinations of Polymyxin B
with Selective Estrogen Receptor Modulators

Yu, Gastrointestinal Tumor 2015
Routy, 2017
Kwa, J Natl Cancer Inst 2016

NUOVE FRONTIERE

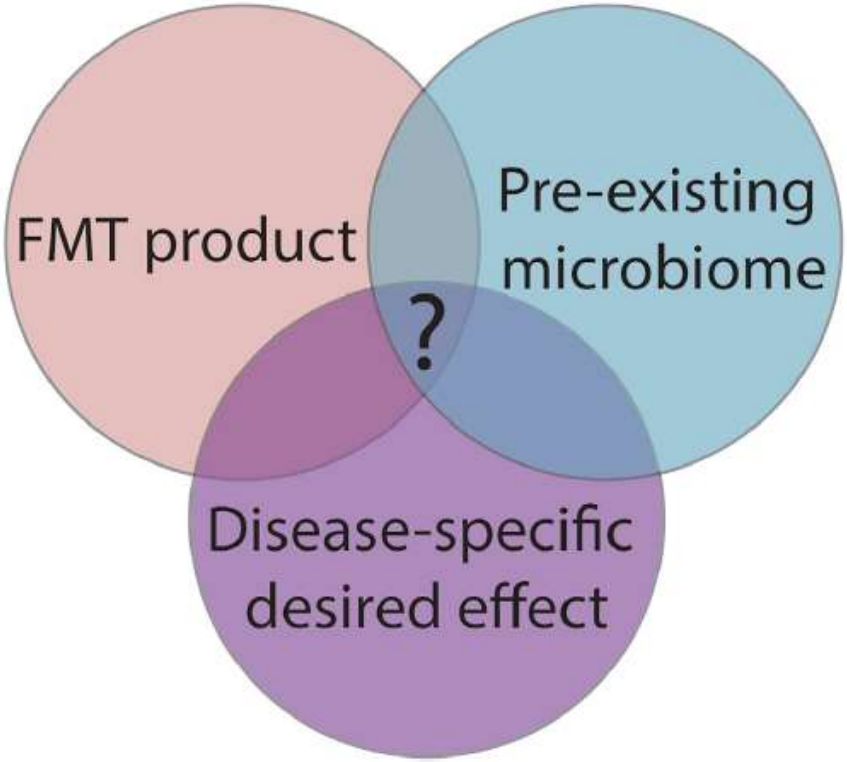
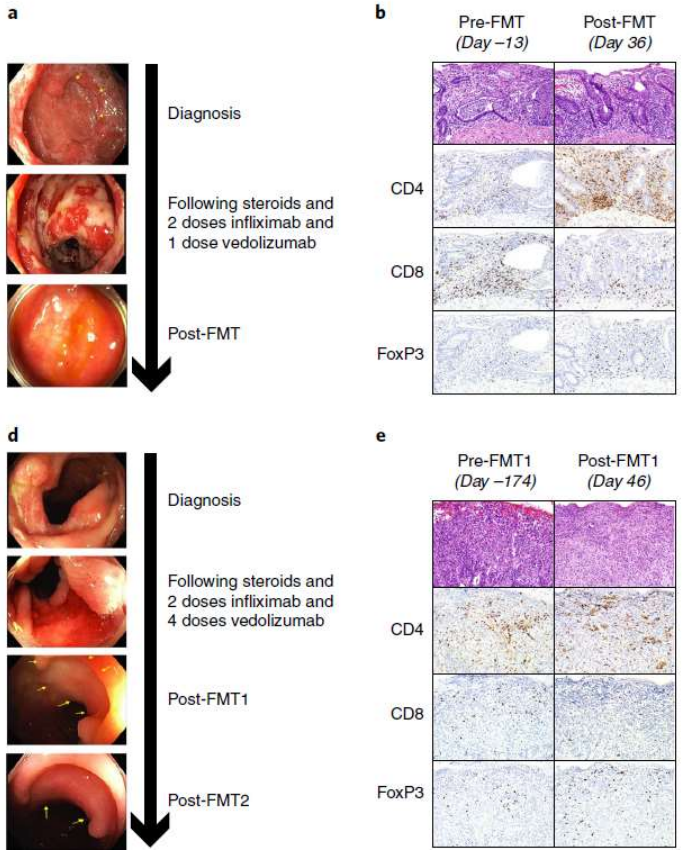
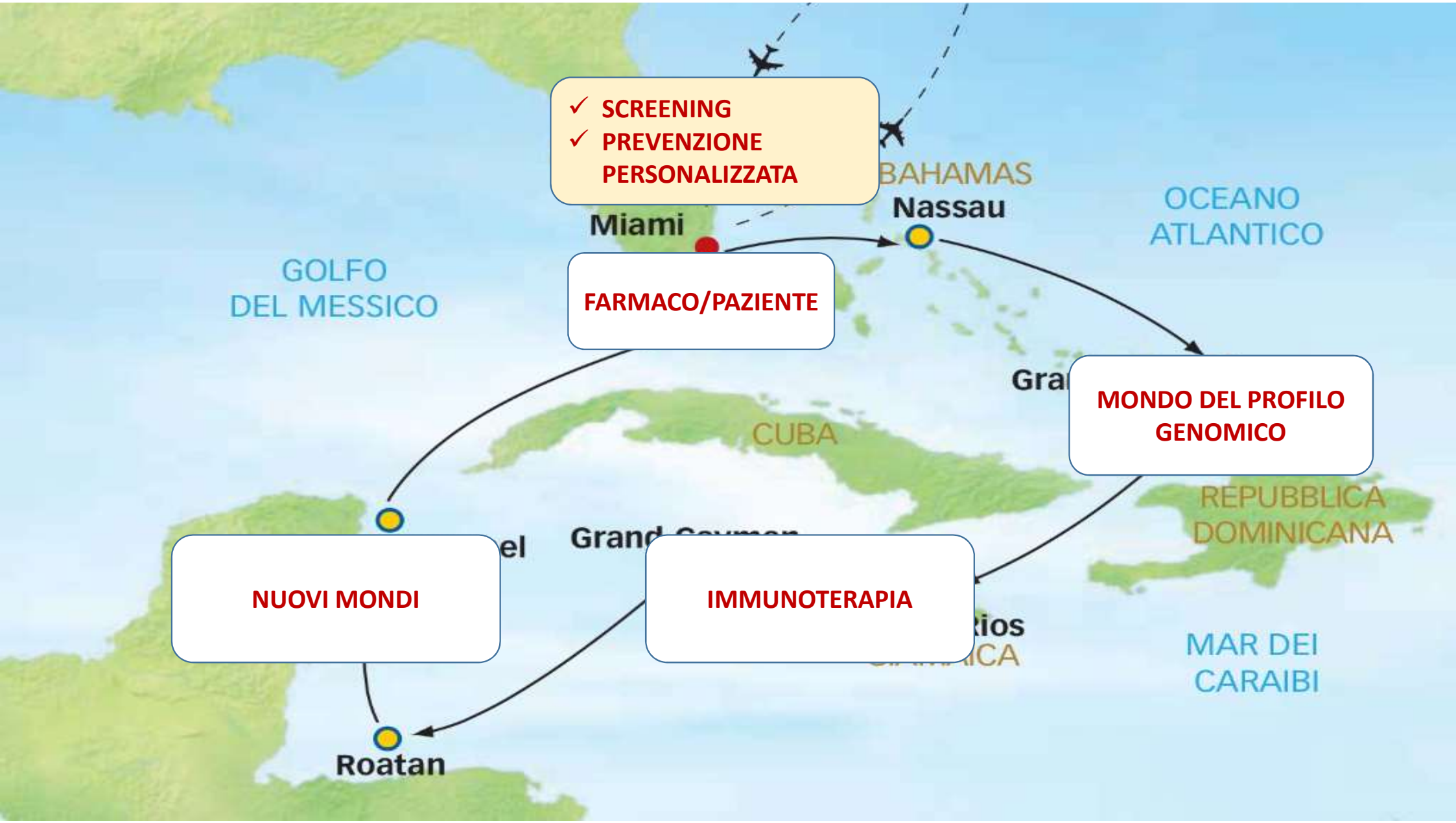


Figure 1. The Challenge of Optimizing FMT
Venn diagram highlighting the intersecting challenges of FMT as a therapy.

nature medicine
BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-018-0238-9

Fecal microbiota transplantation for refractory immune checkpoint inhibitor-associated colitis




✓ SCREENING
✓ PREVENZIONE PERSONALIZZATA
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PREVENZIONE PERSONALIZZATA

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Editorial

Personalized prevention in oncology: integrating the current approaches for the benefit of population health

- Sviluppare nuove metodiche e tecnologie per lo screening e diagnosi precoce (approccio integrato di immagini, tessuti, Biomarcatori e intelligenza artificiale)

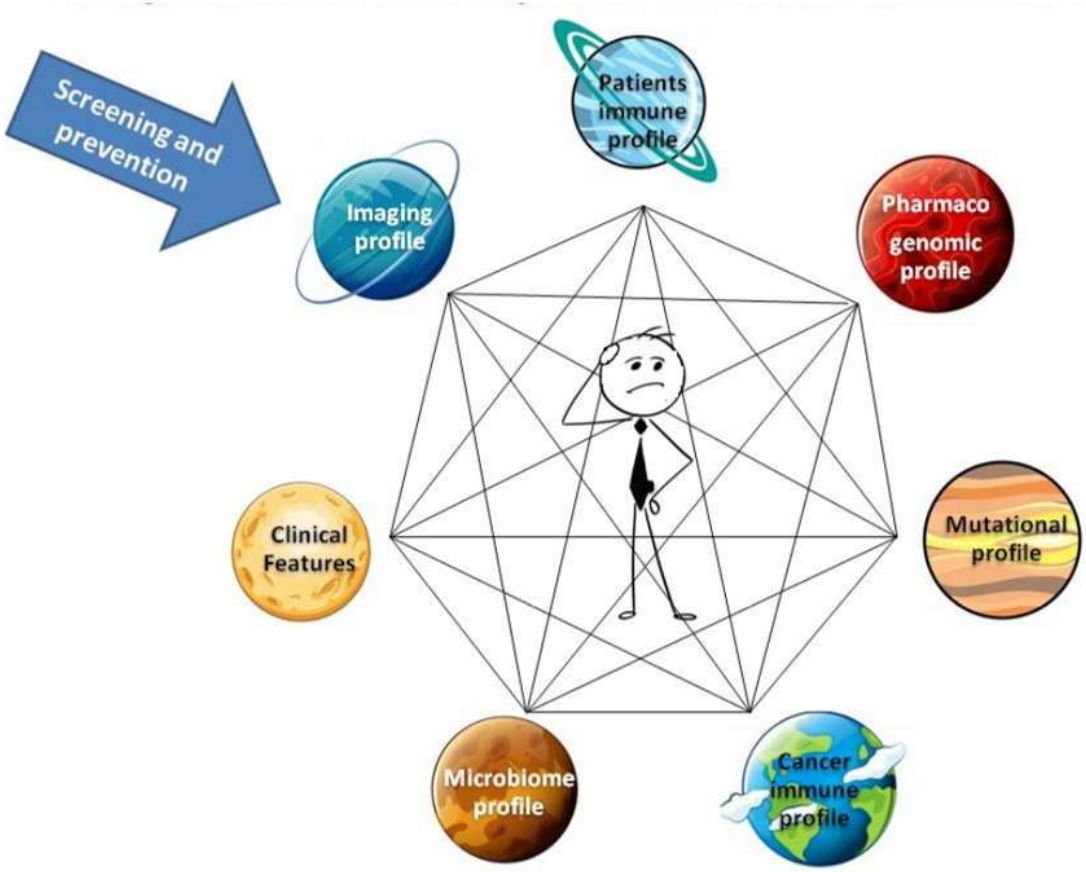
- sviluppare marcatori precoci

Modificare il modificabile

Ecco alcuni dei fattori di rischio modificabili per il tumore al seno, ovvero aspetti sui quali è possibile agire per ridurre la probabilità di ammalarsi:

1. **Sedenterietà**: l'esercizio aiuta a ridurre il rischio;
2. **Sovrappeso / obesità**: i chili in eccesso aumentano sempre il rischio;
3. **Ormoni**: alcune forme di terapia ormonale sostitutiva possono aumentare il rischio;
4. **Storia riproduttiva**; il rischio è più elevato nelle donne che non hanno figli, hanno partorito dopo i 30 anni e non hanno allattato al seno;
5. **Consumo di alcol**: per ridurre il rischio meglio evitare di consumare alcol in eccesso.

INTEGRATIVE PROFILE



GRAZIE PER L'ATTENZIONE