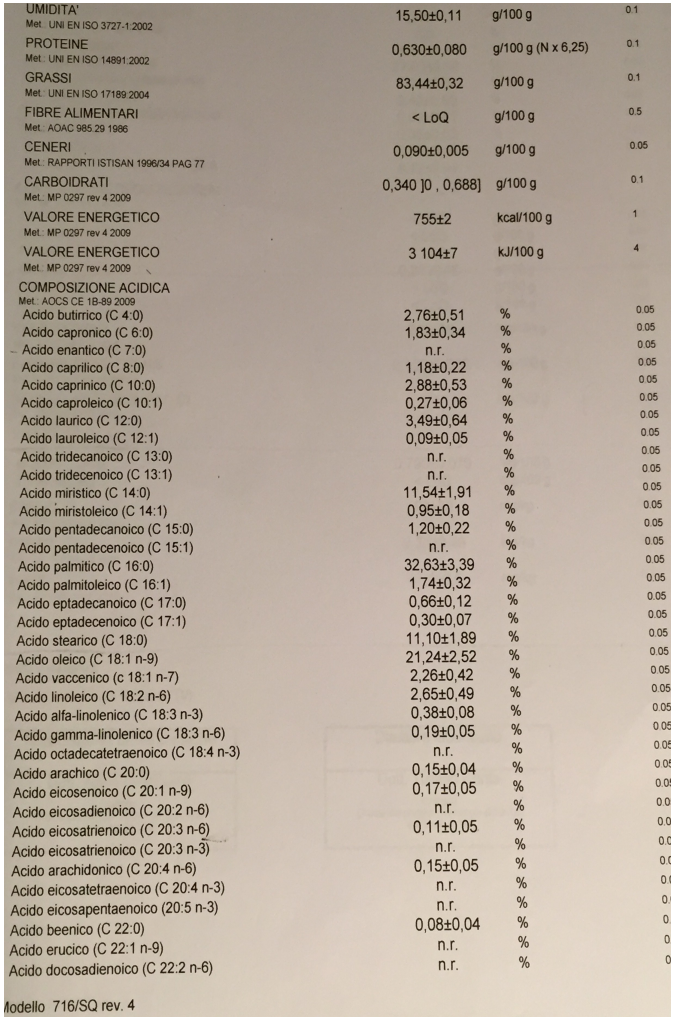
GENOMICA del BURRO

Pier Luigi Rossi
Medico Specialista Scienza della Alimentazione
Docente Università Bologna

BURRO
alimento mediterraneo



UMIDITA' Met.: UNI EN ISO 3727-1:2002	15,50±0,11	g/100 g	0.1
PROTEINE Met.: UNI EN ISO 14891:2002	0,630±0,080	g/100 g (N x 6,25)	0.1
GRASSI Met.: UNI EN ISO 17189:2004	83,44±0,32	g/100 g	0.1
FIBRE ALIMENTARI Met.: AOAC 985.29 1986	< LoQ	g/100 g	0.5
CENERI Met.: RAPPORTI ISTISAN 1996/34 PAG 77	0,090±0,005	g/100 g	0.05
CARBOIDRATI Met.: MP 0297 rev 4 2009	0,340]0 , 0,688]	g/100 g	0.1
VALORE ENERGETICO Met.: MP 0297 rev 4 2009	755±2	kcal/100 g	1
VALORE ENERGETICO Met.: MP 0297 rev 4 2009	3 104±7	kJ/100 g	4
COMPOSIZIONE ACIDICA Met.: AOCS CE 1B-89 2009			
Acido butirrico (C 4:0)	2,76±0,51	%	0.05
Acido capronico (C 6:0)	1,83±0,34	%	0.05
Acido enantico (C 7:0)	n.r.	%	0.05
Acido caprilico (C 8:0)	1,18±0,22	%	0.05
Acido caprinico (C 10:0)	2,88±0,53	%	0.05
Acido caproleico (C 10:1)	0,27±0,06	%	0.05
Acido laurico (C 12:0)	3,49±0,64	%	0.05
Acido lauroleico (C 12:1)	0,09±0,05	%	0.05
Acido tridecanoico (C 13:0)	n.r.	%	0.05
Acido tridecenoico (C 13:1)	n.r.	%	0.05
Acido miristico (C 14:0)	11,54±1,91	%	0.05
Acido miristoleico (C 14:1)	0,95±0,18	%	0.05
Acido pentadecanoico (C 15:0)	1,20±0,22	%	0.05
Acido pentadecenoico (C 15:1)	n.r.	%	0.05
Acido palmitico (C 16:0)	32,63±3,39	%	0.05
Acido palmitoleico (C 16:1)	1,74±0,32	%	0.05
Acido eptadecanoico (C 17:0)	0,66±0,12	%	0.05
Acido eptadecenoico (C 17:1)	0,30±0,07	%	0.05
Acido stearico (C 18:0)	11,10±1,89	%	0.05
Acido oleico (C 18:1 n-9)	21,24±2,52	%	0.05
Acido vaccenico (c 18:1 n-7)	2,26±0,42	%	0.05
Acido linoleico (C 18:2 n-6)	2,65±0,49	%	0.05
Acido alfa-linolenico (C 18:3 n-3)	0,38±0,08	%	0.05
Acido gamma-linolenico (C 18:3 n-6)	0,19±0,05	%	0.05
Acido octadecatetraenoico (C 18:4 n-3)	n.r.	%	0.05
Acido arachico (C 20:0)	0,15±0,04	%	0.05
Acido eicosenoico (C 20:1 n-9)	0,17±0,05	%	0.05
Acido eicosadienoico (C 20:2 n-6)	n.r.	%	0.0
Acido eicosatrienoico (C 20:3 n-6)	0,11±0,05	%	0.0
Acido eicosatrienoico (C 20:3 n-3)	n.r.	%	0.0
Acido arachidonico (C 20:4 n-6)	0,15±0,05	%	0.0
Acido eicosatetraenoico (C 20:4 n-3)	n.r.	%	0.0
Acido eicosapentaenoico (20:5 n-3)	n.r.	%	0.0
Acido beenico (C 22:0)	0,08±0,04	%	0.0
Acido erucico (C 22:1 n-9)	n.r.	%	0.0
Acido docosadienoico (C 22:2 n-6)	n.r.	%	0.0

Modello 716/SQ rev. 4

- **Ho analizzato 45 molecole lipidiche e 15 molecole tra vitamine, minerali e altre componenti del burro.**
- **Il burro è un alimento caratterizzato da una presenza complessa e varia di acidi grassi: a catena corta, monoinsaturi, saturi e polinsaturi.**
- **Le componenti lipidiche del burro possono svolgere una azione di genomica nutrizionale sul DNA cellule umane e batteriche (microbiota intestinale)**

MODULAZIONE GENICA
ACIDI GRASSI

MODULAZIONE GENICA

genomica nutrizionale è lo studio degli effetti di molecole alimentari sul DNA

EPIGENETICA NUTRIGENOMICA NUTRACEUTICA

MODULAZIONE GENICA

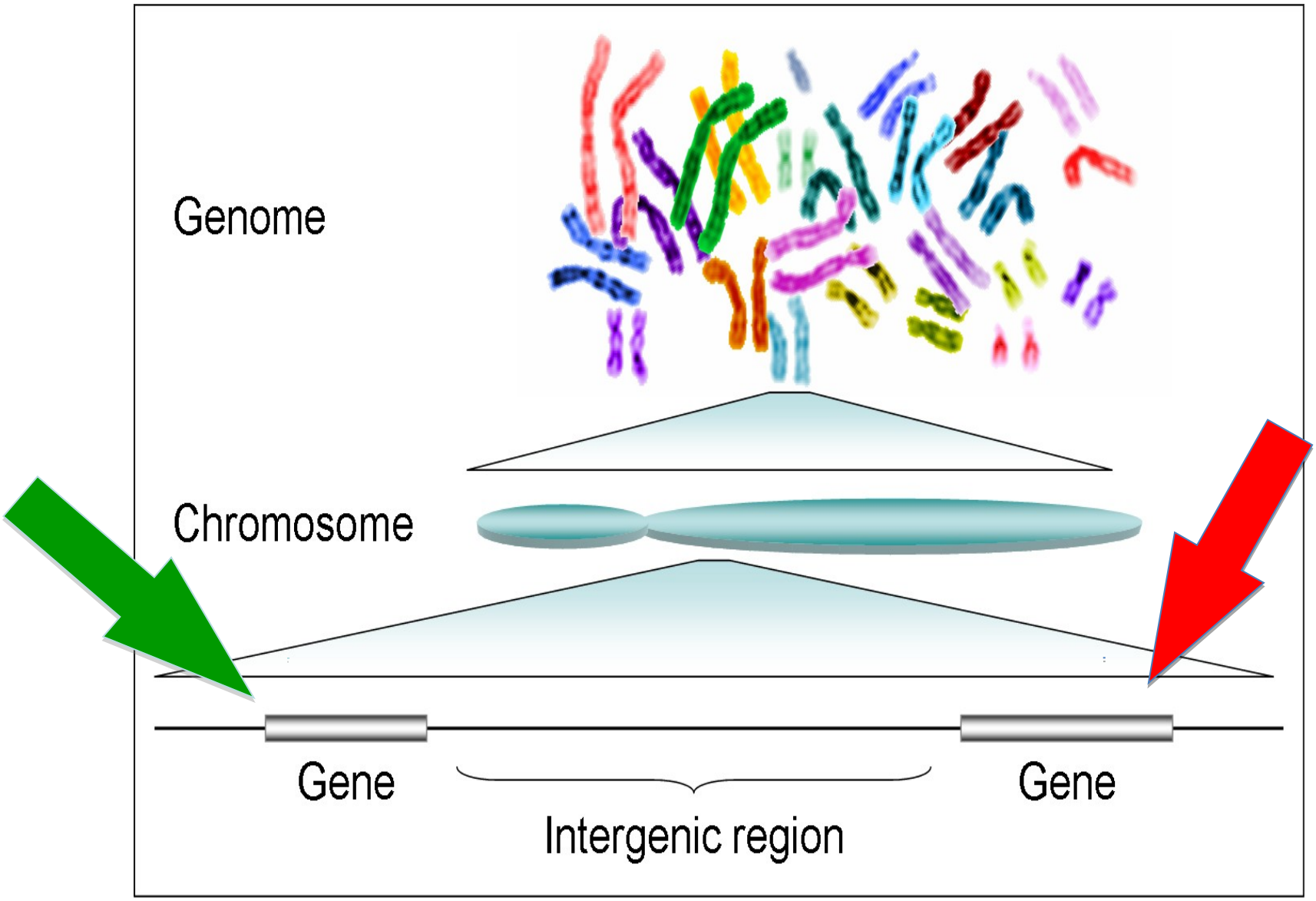
MODULATORI GENICI

FENOTIPO

SOFTWARE
MOLECOLE

HARDWARE
DNA

MODULAZIONE GENICA



EPIGENETICA APE REGINA

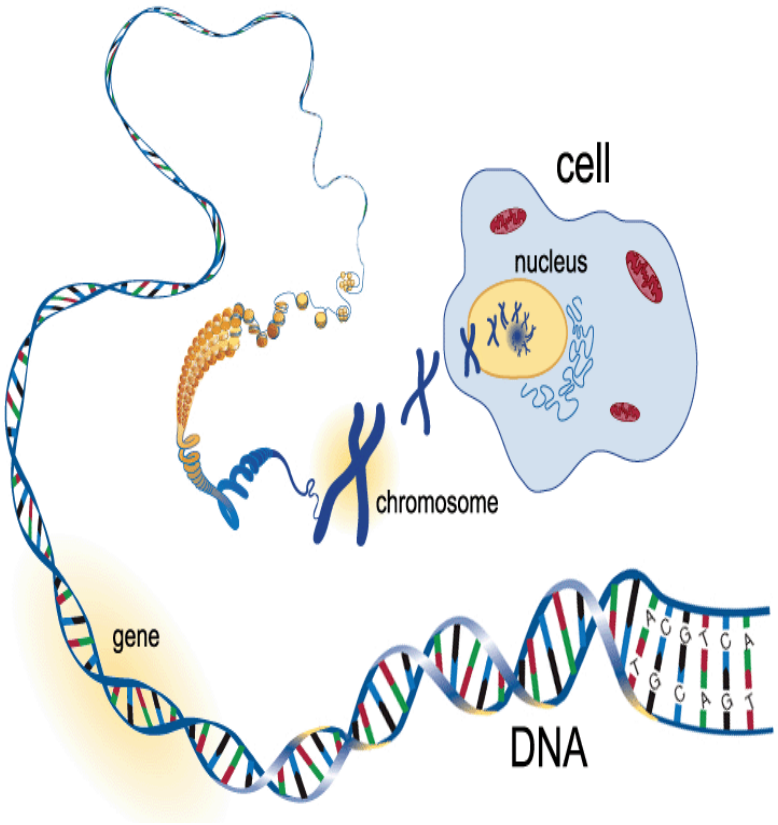
Kucharski R. et al. Science, 2008

La pappa reale è nutrimento
per le LARVE (fino a tre giorni di età)
per l'APE REGINA (per tutta la vita).

GENOTIPO
DNA COSTANTE

FENOTIPO
VARIABILE

GENOMA e OBESITA'
dalle CALORIE alle MOLECOLE



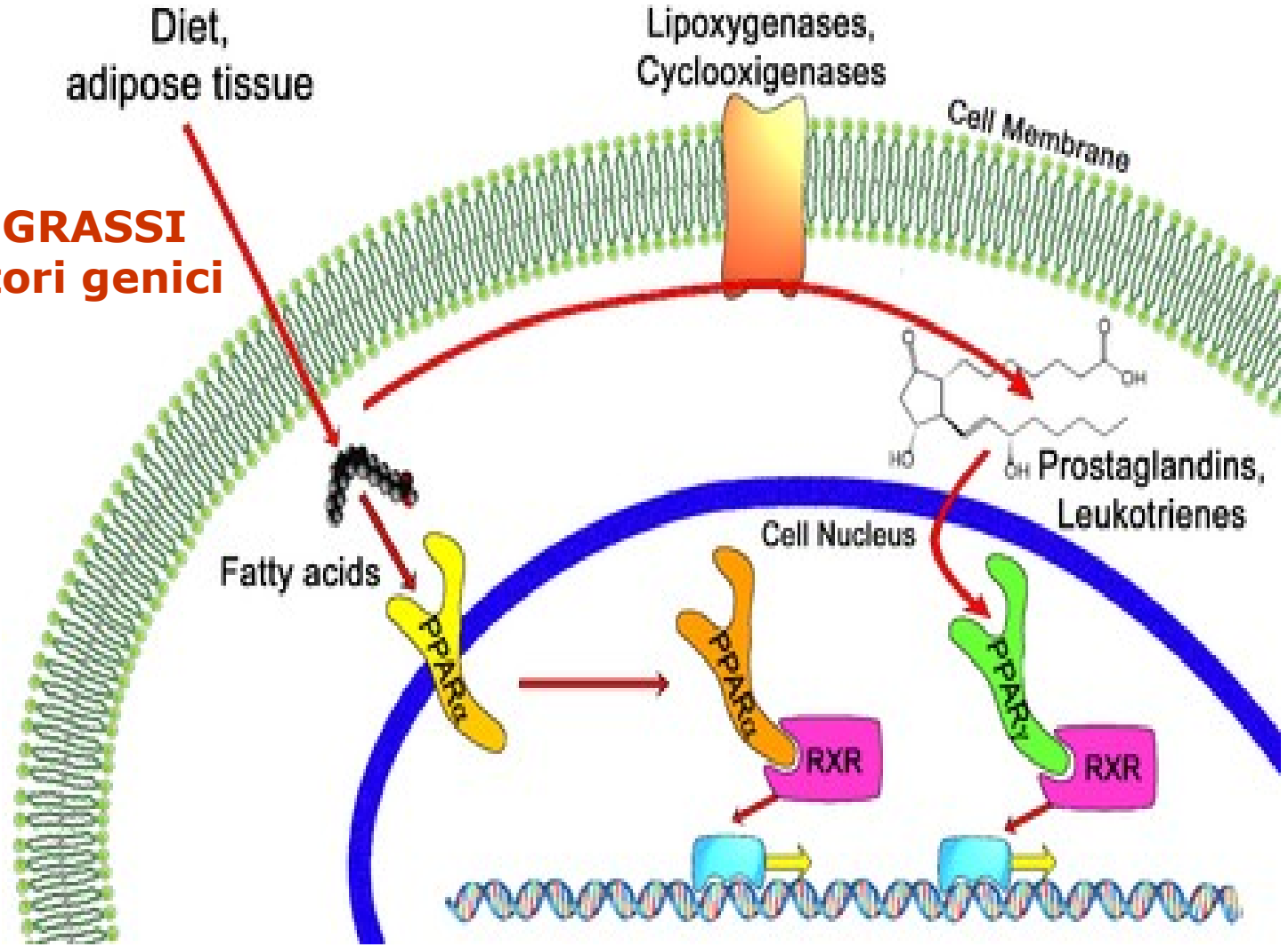
Nessuna Caloria agisce sui geni

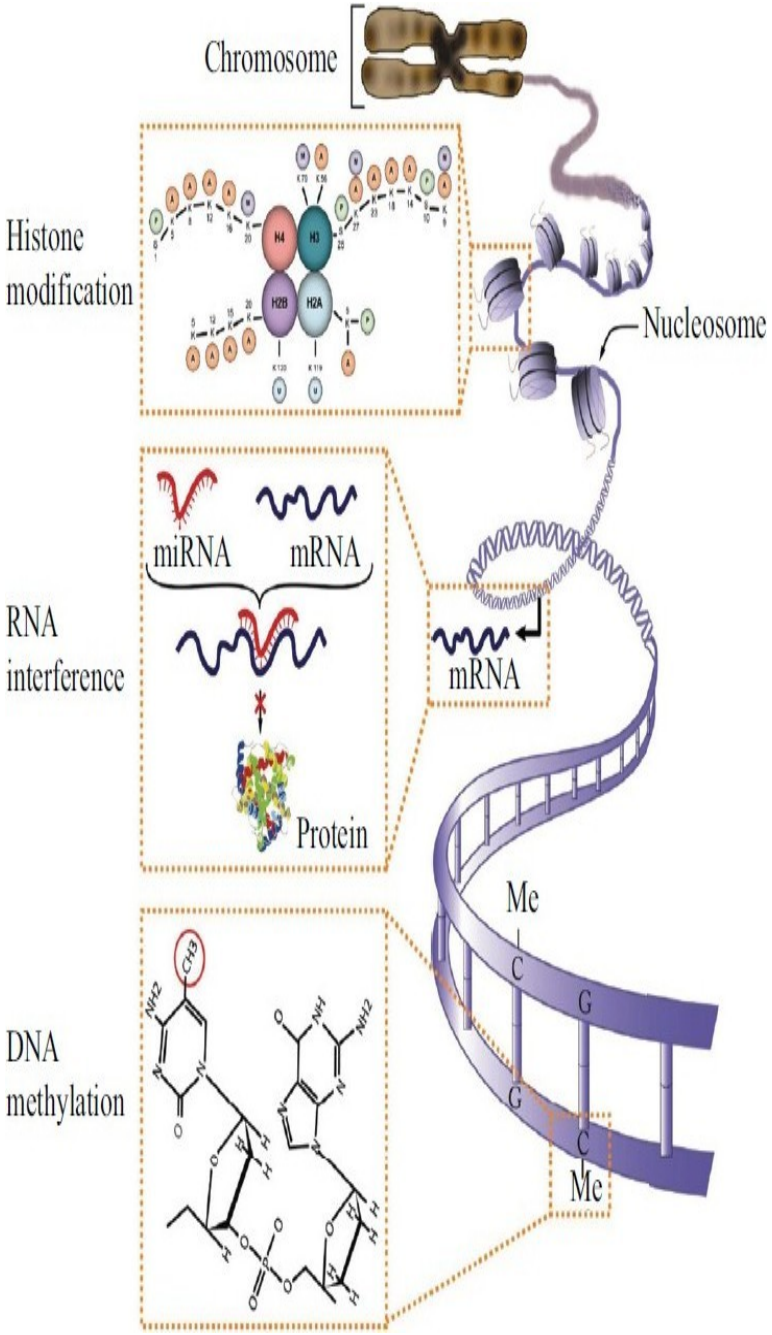
SOLO LE MOLECOLE HANNO QUESTA AZIONE sul DNA

IL CIBO E' IL PRINCIPALE MEDIATORE TRA AMBIENTE E DNA

EPOCA GENOMICA

ACIDI GRASSI
modulatori genici





GENOMICA BURRO

Gli acidi grassi a catena corta SCFA (Short Chain Fatty Acids) costituiscono il 12.5 % del burro.

Sono capaci di svolgere una azione di inibizione delle istone deacetilasi (Histone deacetylase inhibitors HDACi's), stabilizzando il DNA cellulare.

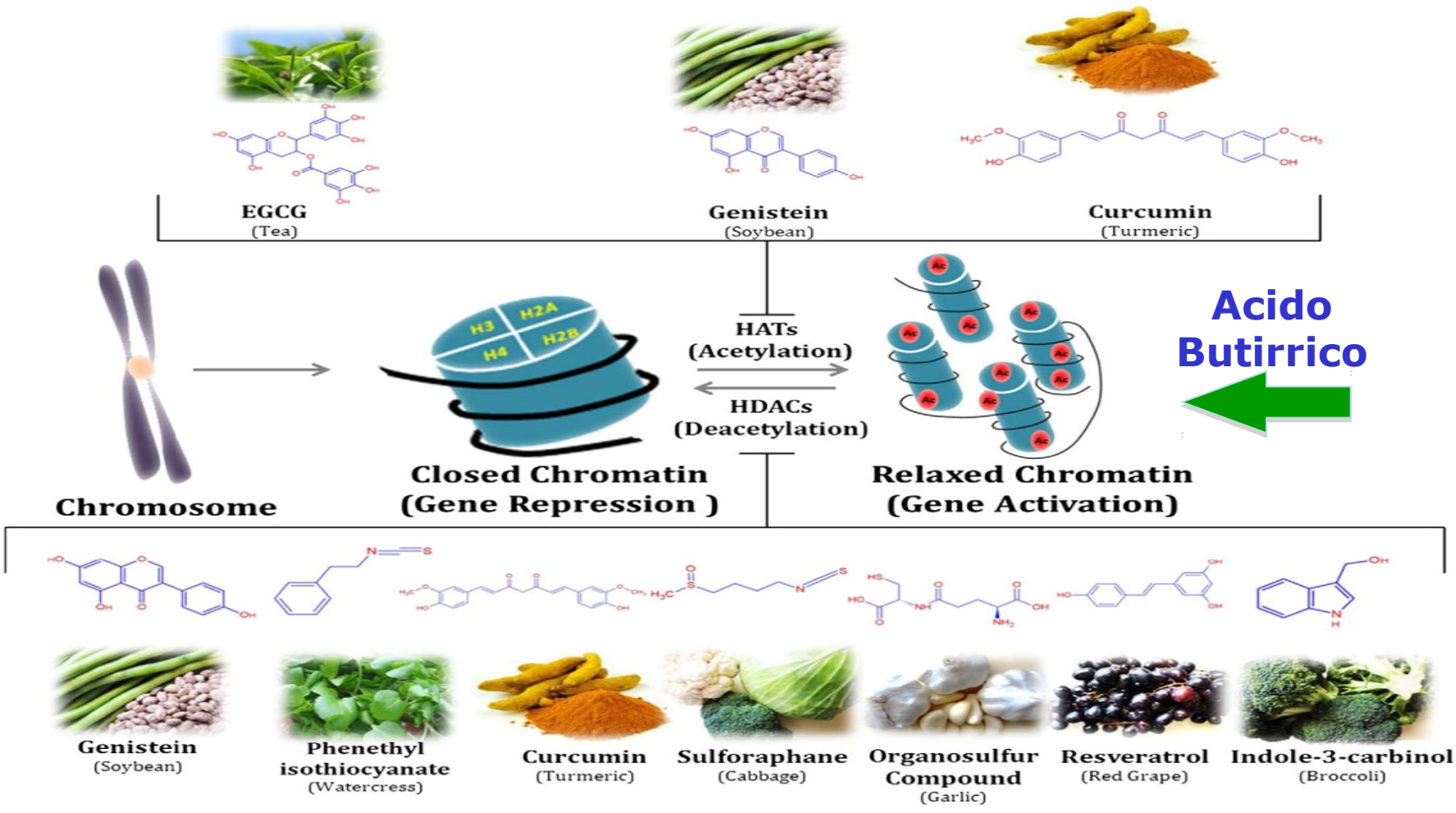
In particolare ACIDO BUTIRRICO !

principali meccanismi epigenetici

ACIDI GRASSI A CATENA CORTA
Numero di carbonio inferiore a 12 atomi

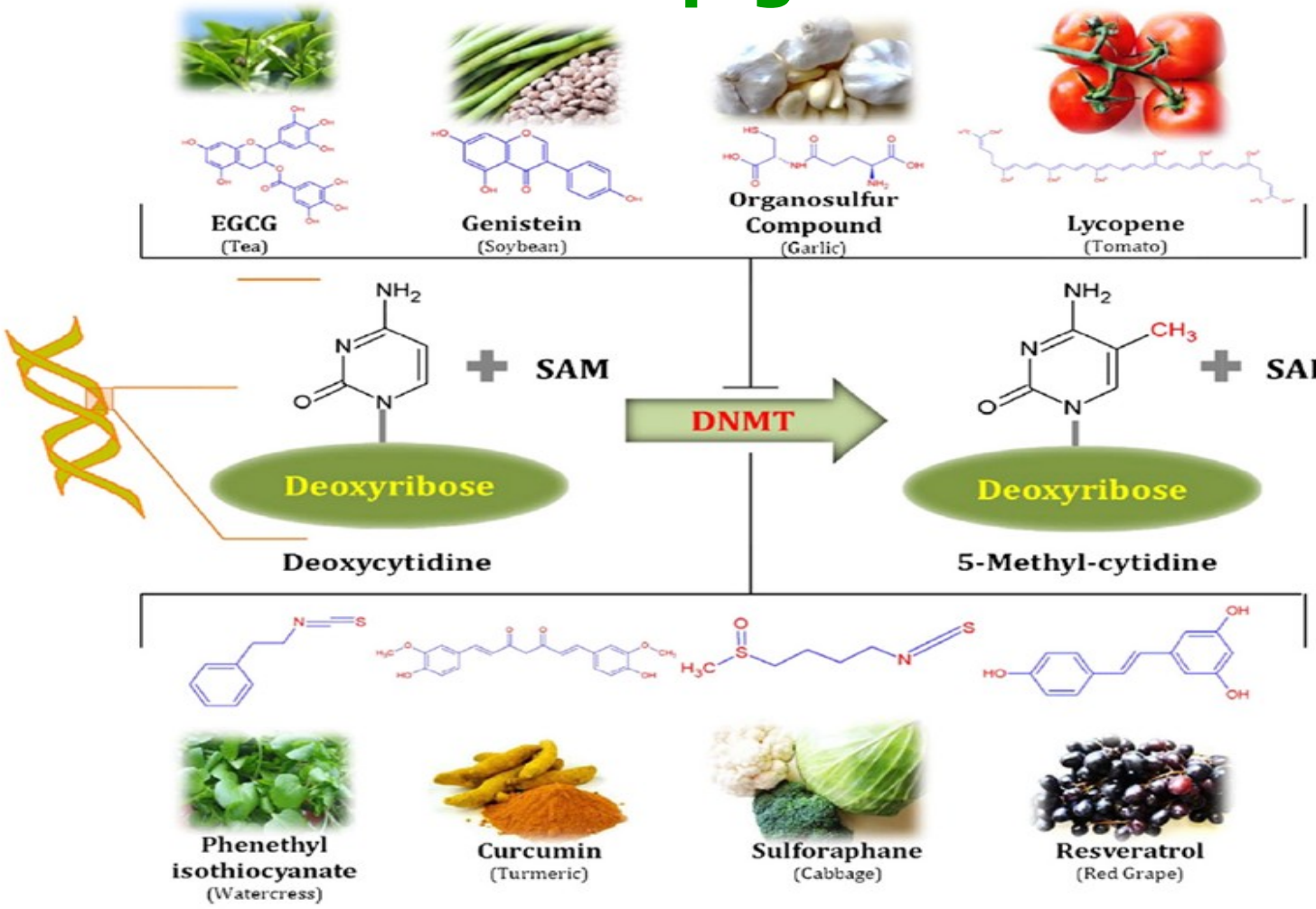
4:0	ACIDO BUTIRRICO	acido butanoico	$C_4H_8O_2$ $CH_3(CH_2)_2COOH$
5:0	acido valerico	acido pentanoico	$C_5H_{10}O_2$ $CH_3(CH_2)_3COOH$
6:0	acido caproico	acido esanoico	$C_6H_{12}O_2$ $CH_3(CH_2)_4COOH$
7:0	acido enantico	acido eptanoico	$C_7H_{14}O_2$ $CH_3(CH_2)_5COOH$
8:0	acido caprilico	acido ottanoico	$C_8H_{16}O_2$ $CH_3(CH_2)_6COOH$
9:0	acido pelargonico	acido nonanoico	$C_9H_{18}O_2$ $CH_3(CH_2)_7COOH$
10:0	acido caprinico	acido decanoico	$C_{10}H_{20}O_2$ $CH_3(CH_2)_8COOH$
11:0	acido undecanoico		$C_{11}H_{22}O_2$ $CH_3(CH_2)_9COOH$
12:0	acido laurico	acido dodecanoico	$C_{12}H_{24}O_2$ $CH_3(CH_2)_{10}COOH$

MODULATORI GENICI
epigenetica



S. Shankar et al. / Pharmacology & Therapeutics 138 (2013) 1–17

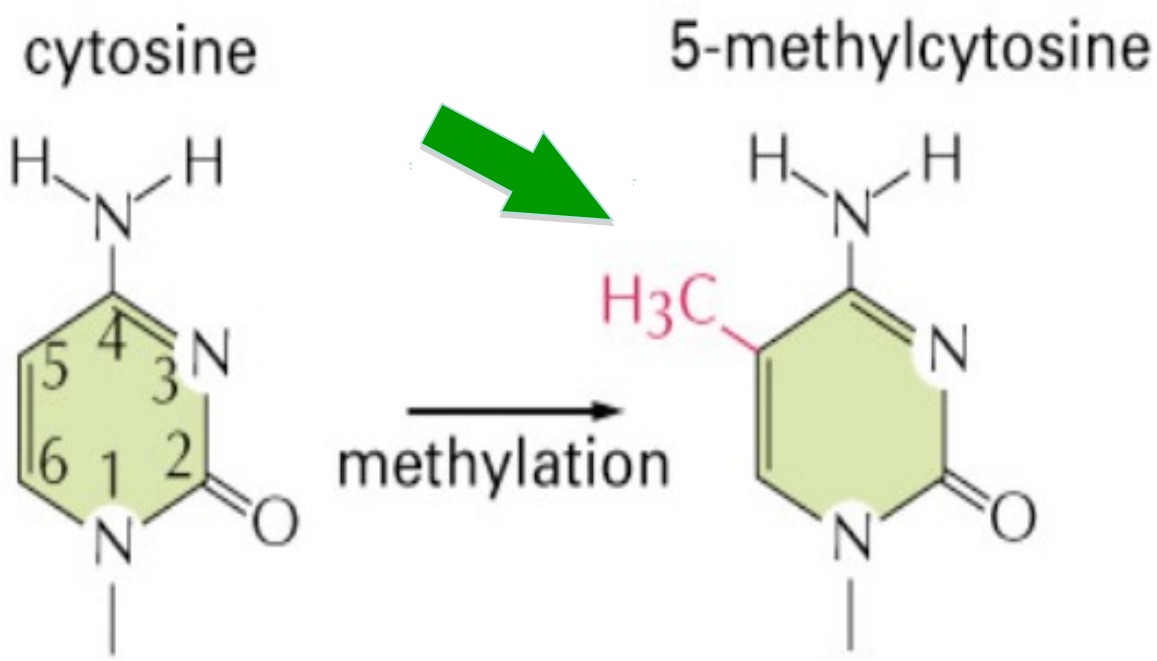
MODULATORI GENICI
epigenetica



ACIDO BUTIRRICO

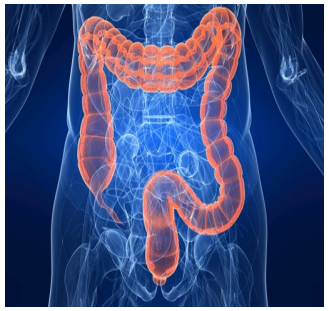
S. Shankar et al. / Pharmacology & Therapeutics 138 (2013) 1–17

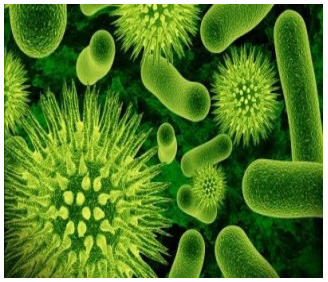
METILAZIONE
gruppo metile –CH3

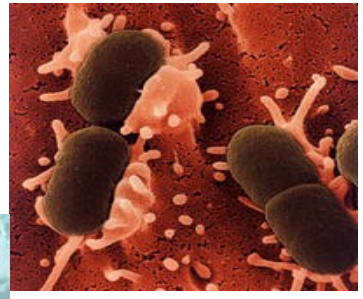


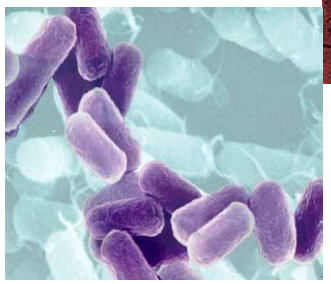
OMOCISTEINA
VITAMINA B12 - ACIDO FOLICO

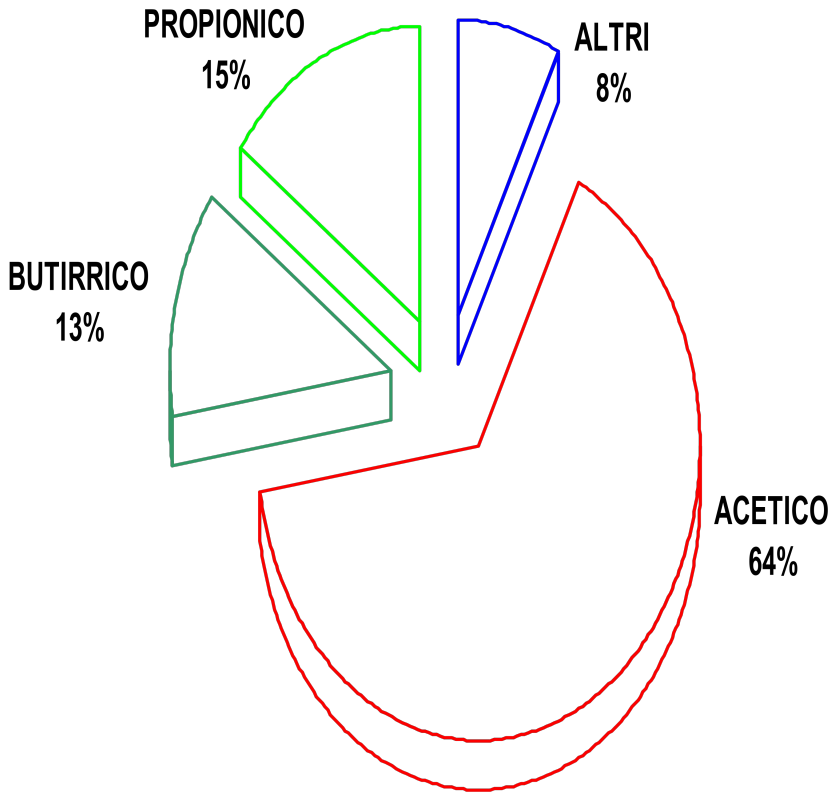
FIBRA IDROSOLUBILE
ACIDI GRASSI a CATENA CORTA











acido butirrico svolge modulazione genica
cellule colon e batteri microbiota

BUTIRRATO
modulazione genica

- JP. "Istone deacetilasi inibitori: una nuova classe di potenziali agenti terapeutici per il trattamento del cancro." Clin Cancer Res (2002). 8 (3): 662-4.
- Richon VM, O'Brien JP. "Histone deacetylase inhibitors: a new class of potential therapeutic agents for cancer treatment." Clin Cancer Res (2002). 8(3): 662-4.
- Bora-Tatar G. Dayangaç-Erden D. Demir AS, et al. Molecular modifications on carboxylic acid derivatives as potent histone deacetylase inhibitors: Activity and docking studies. Bioorg Med Chem. 2009;17:5219
- J cellular Biochem 2015 Maggio; 116 (5): 797-808. doi: 10.1002 / jcb.25036.
  Modulazione reciproca degli inibitori dell'istone deacetilasi butirrato di sodio e tricostatin A sul metabolismo energetico delle cellule del cancro al seno.
  Rodrigues MF, Carvalho E...
- Histone Deacetylase Inhibitors in Clinical Studies as Templates for New Anticancer Agents Madhusoodanan Mottamal 1,2,*, Shilong Zheng 1,2, Tien L. Huang 1,3 and Guangdi Wang 1,2

MAGGIO 2015

Li et al. BMC Biochemistry (2015) 16:2
DOI 10.1186/s12858-014-0030-5

BMC Biochemistry

RESEARCH ARTICLE Open Access

Histone deacetylase inhibitor sodium butyrate suppresses DNA double strand break repair induced by etoposide more effectively in MCF-7 cells than in HEK293 cells

Liping Li[1,2*†], Youxiang Sun[1,2†], Jiangqin Liu[1], Xiaodan Wu[1,2], Lijun Chen[1,2], Li Ma[1] and Pengfei Wu[1,2]

Abstract

Background: Histone deacetylase inhibitors (HDACi's) are emerging as promising anticancer drugs alone or in combination with chemotherapy or radiotherapy agents. Previous research suggests that HDACi's have a high degree of selectivity for killing cancer cells, but little is known regarding the impact of different cellular contexts on HDACi treatment. It is likely that the molecular mechanisms of HDACi's involve processes that depend on the chromatin template, such as DNA damage and repair. We sought to establish the connection between the HDACi sodium butyrate and DNA double-strand break (DSB) damage in human breast cancer MCF-7 and non-cancerous human embryonic kidney293 (HEK293) cells.

Results: Sodium butyrate inhibited the proliferation of both HEK293 and MCF-7 cells in a dose- and time- dependent manner, but the effects on MCF-7 cells were more obvious. This differential effect on cell growth was not explained by differences in cell cycle arrest, as sodium butyrate caused an arrest in G_1/G_2 phase and a decrease in S phase for both cell lines. At high doses of sodium butyrate or in combination with etoposide, MCF-7 cells formed fewer colonies than HEK293 cells. Furthermore, sodium butyrate enhanced the formation of etoposide-induced γ-H2AX foci to a greater extent in MCF-7 than in HEK293 cells. The two cells also displayed differential patterns in the nuclear expression of DNA DSB repair proteins, which could, in part, explain the cytotoxic effects of sodium butyrate.

Conclusions: These studies suggest that sodium butyrate treatment leads to a different degree of chromatin relaxation in HEK293 and cancerous MCF-7 cells, which results in differential sensitivity to the toxic effects of etoposide in controlling damaged DNA repair.

Keywords: Double strand breaks, Histone deacetylase inhibitor, MCF-7, HEK293, Etoposide, Sodium butyrate

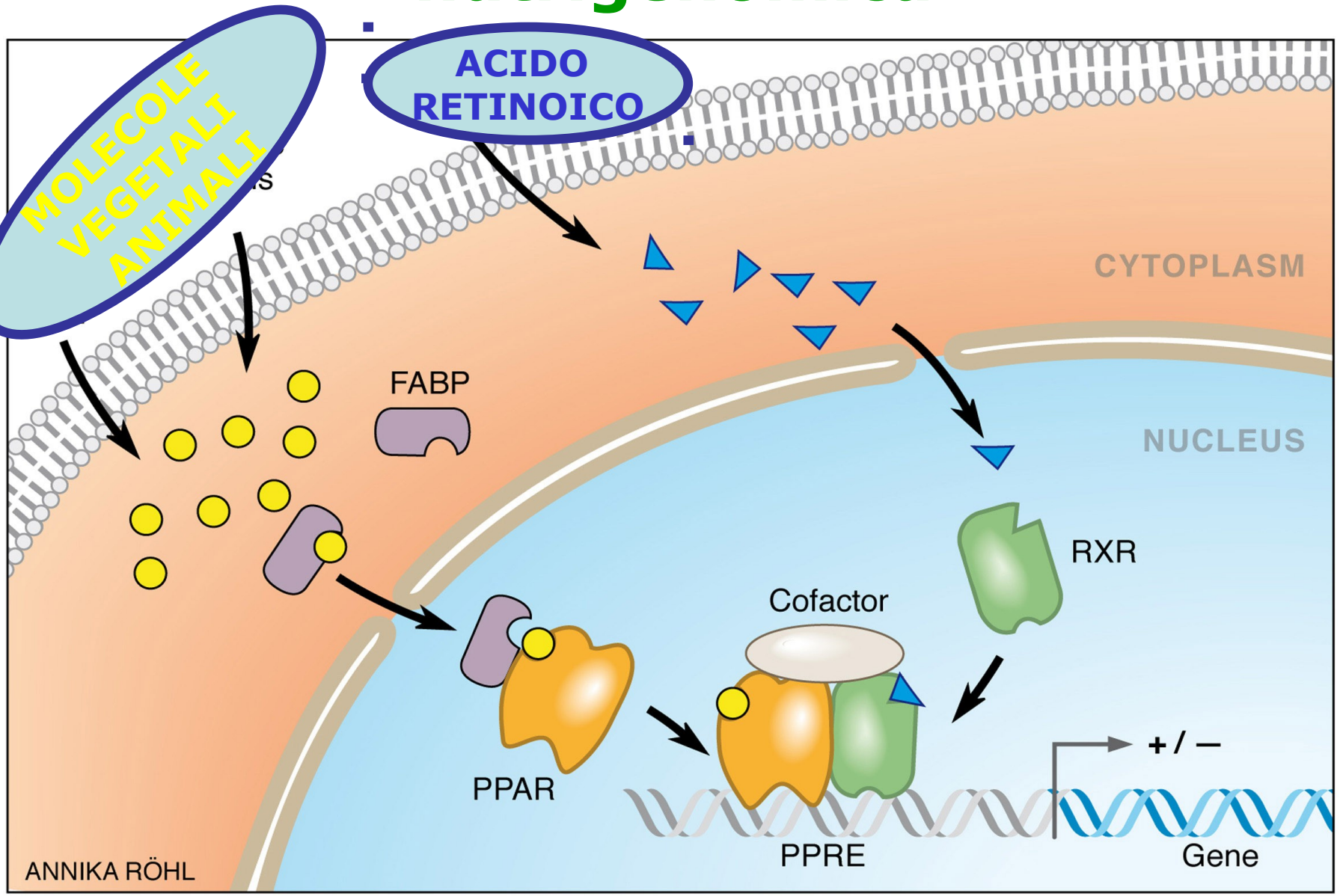
Background

Eukaryotic DNA is bound by histones and organized into chromatin, which serves as the true in vivo substrate of transcription, replication and DNA repair. Post-translational modification of histones alters chromatin structure; for example, histone acetylation plays a central role in the unwinding of DNA. Histone deacetylase inhibitors (HDACi's) globally increase histone acetylation, relaxing chromatin structure and leading to reversible decondensation of chromatin regions [1]. These inhibitors of chromatin-modifying enzymes are emerging as a promising anticancer drug and already have shown anti-cancer effects in both pre-clinical and clinical settings [2,3]. HDACi's are gaining increasing attention because of their therapeutic effectiveness in selectively killing cancer cells and their mild toxicity profile [3-5].

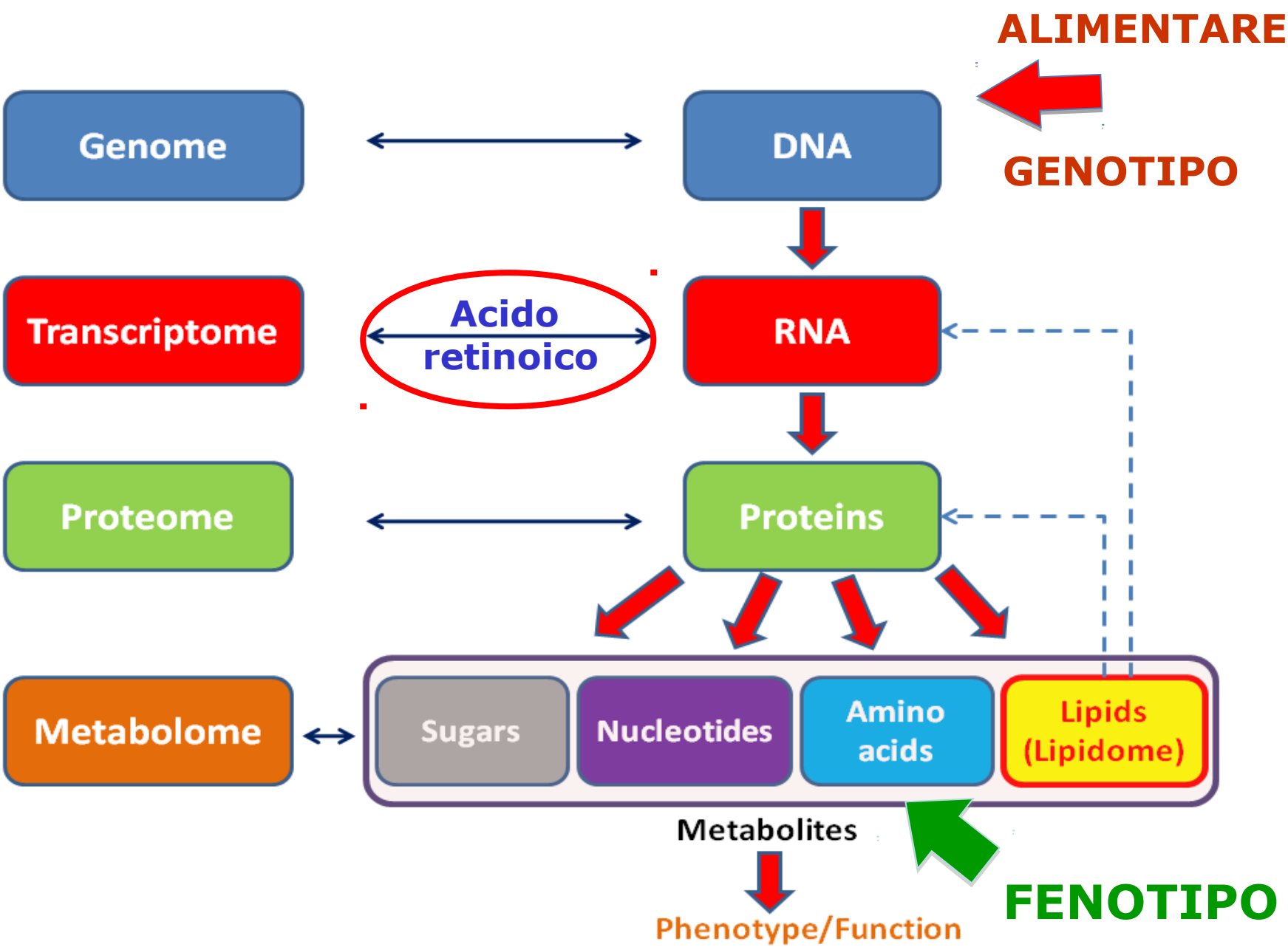
Double strand breaks (DSBs) in DNA occur naturally in the genome during replication and are increased by exogenous DNA damaging agents. Many anti-cancer therapeutics, including radiotherapy and chemotherapy agents, kill tumor cells by inducing DSBs. DSB repair is

* Correspondence: lipinggdmc@126.com
†Equal contributors
[1]Key Laboratory for Medical Molecular Diagnostics of Guangdong Province, Guangdong Medical College, Xincheng Road, Dongguan 523808, P R China
[2]Department of Biochemistry, School of Basic Medicine, Guangdong Medical College, Dongguan 523808, P R China

MODULAZIONE GENICA
nutrigenomica



MODULAZIONE GENICA



ACIDO RETINOICO
ATTIVA I RECETTORI NUCLEARI

Recettori degli estrogeni

Recettori del progesterone

Recettore degli androgeni

Recettore degli ormoni tiroidei

Recettore della vitamina D

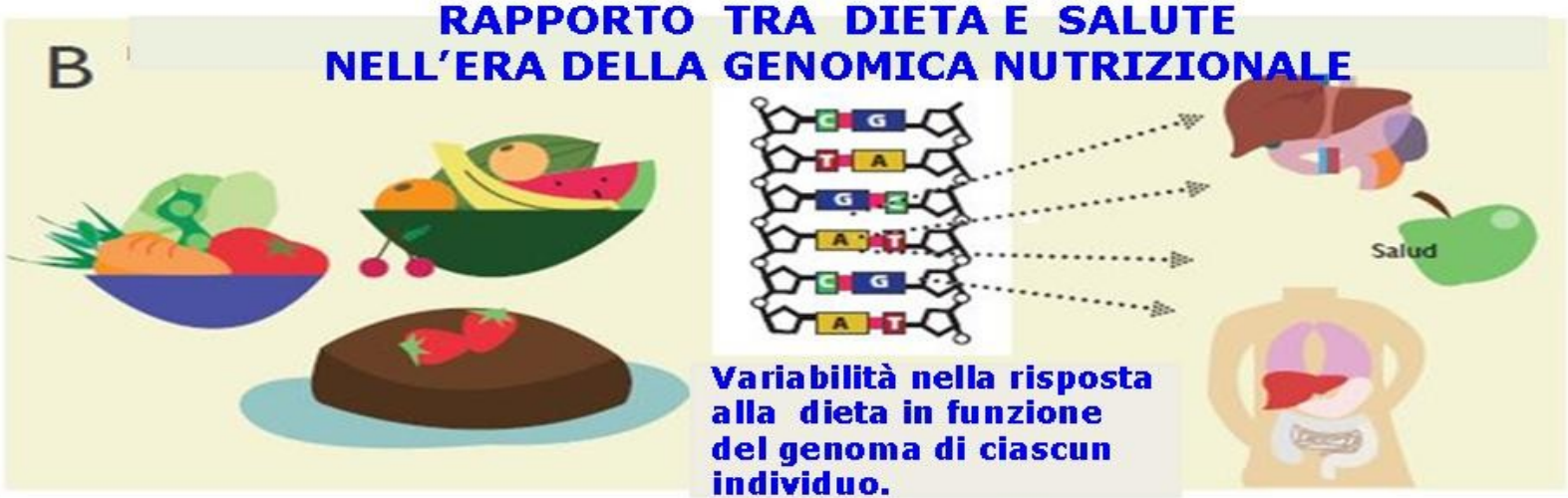
Recettori dell' acido retinoico

Recettori proliferatori e attivatori dei perossisomi (PPARs)

Beta CAROTENE

All – trans - RETINOLO

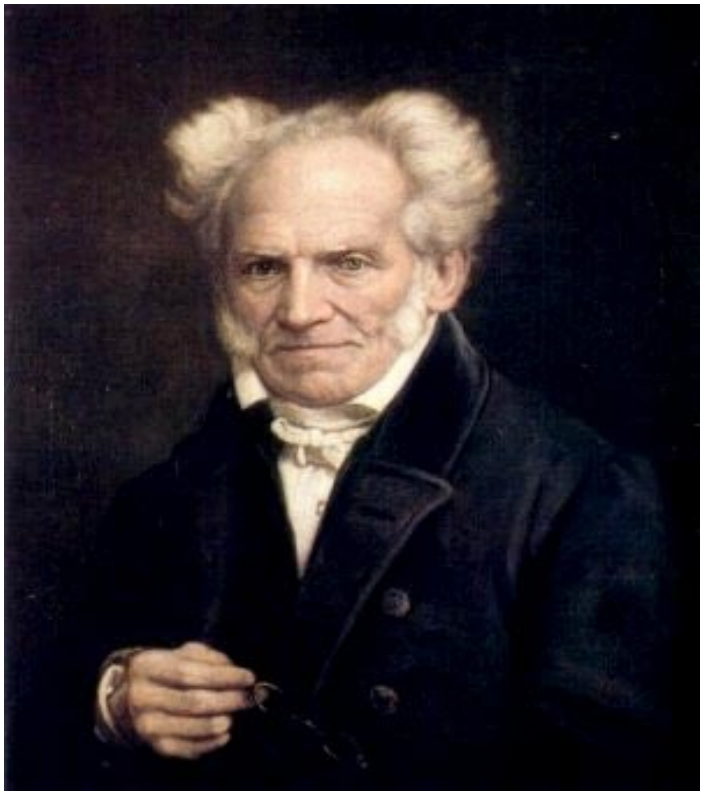
COSA È CAMBIATO con l'era genomica?



sintesi proteica – enzimi- fase post genomica

Non si ha paura
delle idee nuove!

Abbiamo paura
a perdere
le idee vecchie !



Arthur Schopenhauer
22 Febbraio 1788
21 Settembre 1860