

Cancer: From Basic Research to Life Style and Therapy

Prof. Riccardo Alessandro

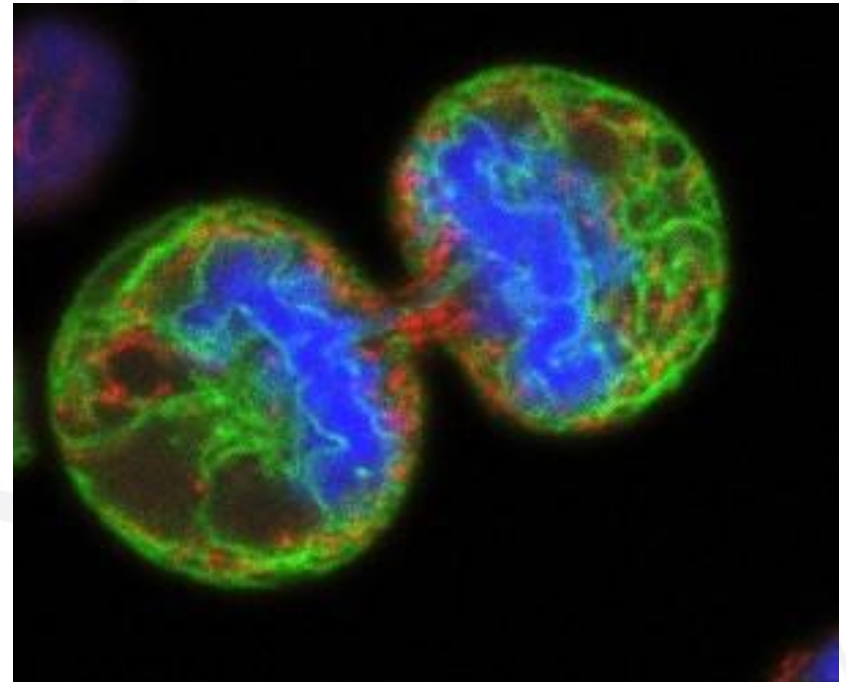
***Department of Biopathology and Biomedical Methodologies
School of Medicine, University of Palermo***

Liceo Classico Vittorio Emanuele II - Palermo 16 Novembre 2016



What is cancer?

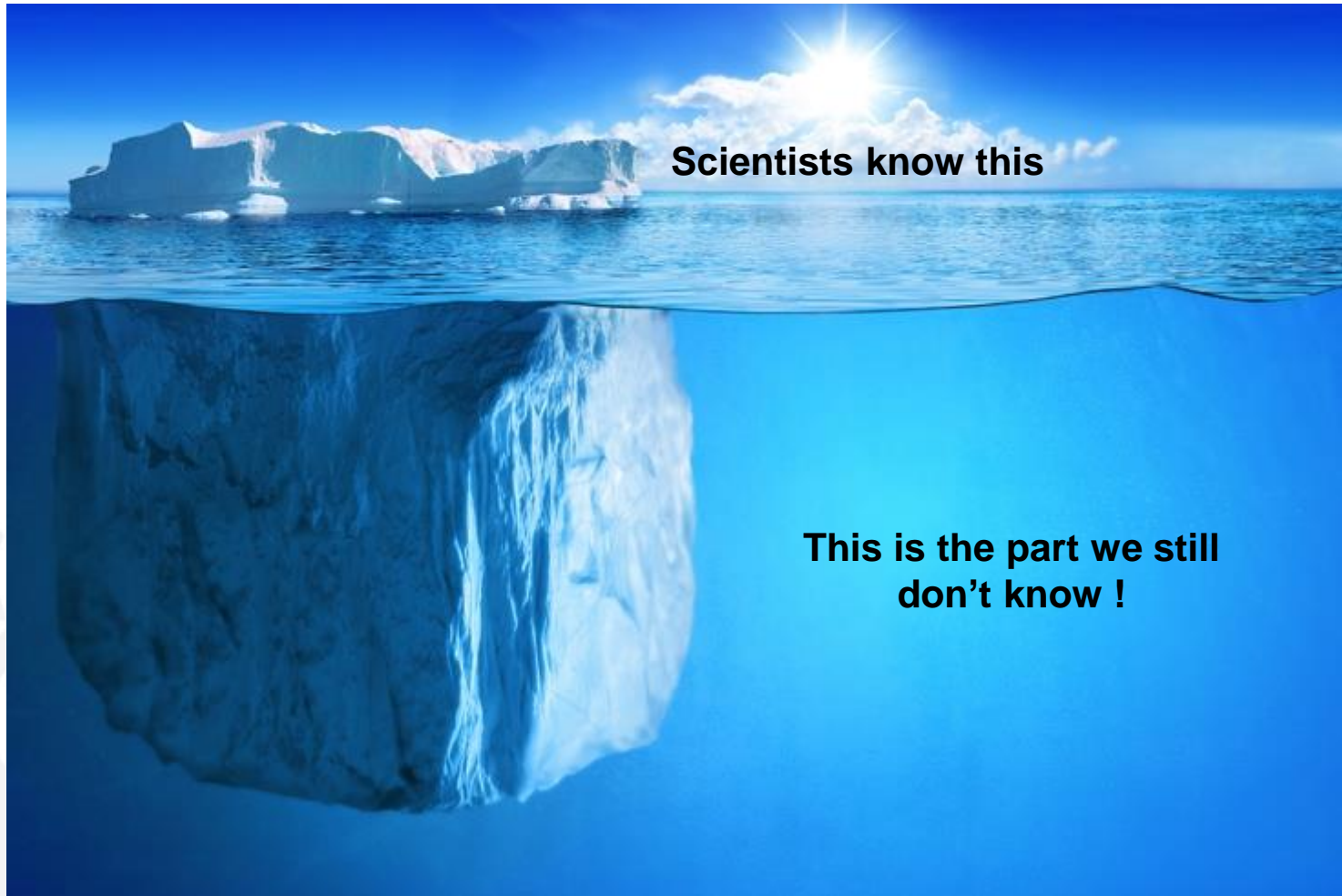
- All cancers derive from single cells that have acquired the characteristics of continually dividing in an unrestrained manner and invading surrounding tissues.
- Cancer cells behave in this abnormal manner because of changes in the DNA sequence of key genes, which are known as cancer genes. Therefore all cancers are genetic diseases.



Human melanoma cell undergoing cell division

Credit: Paul Smith & Rachel Errington, Wellcome Images

Cancer is an iceberg !



Scientists know this

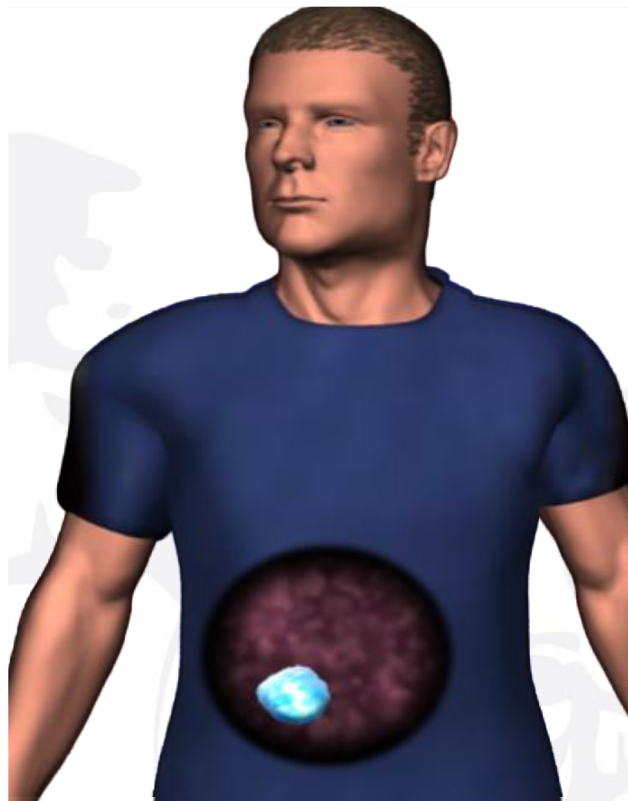
**This is the part we still
don't know !**



THE WATER IS THE RESEARCH !

Cancer progression

Mutations in multiple cancer genes are required for the development and progression of a single cancer



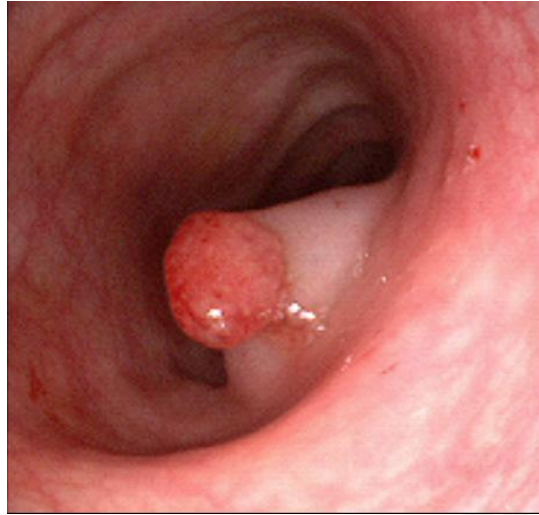
Benign Tumour

In situ cancer

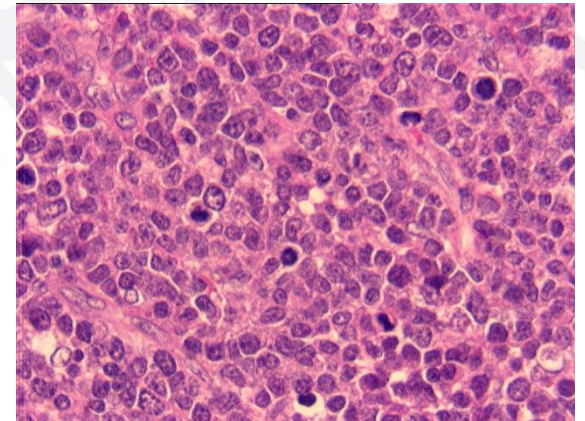
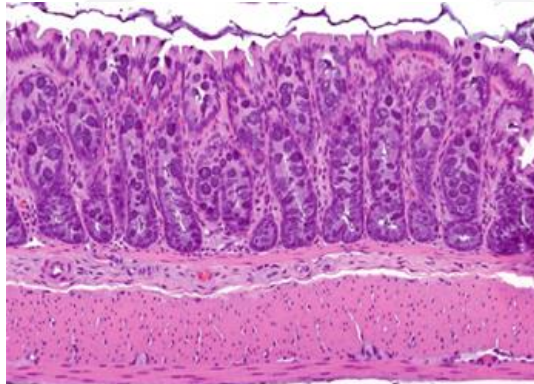
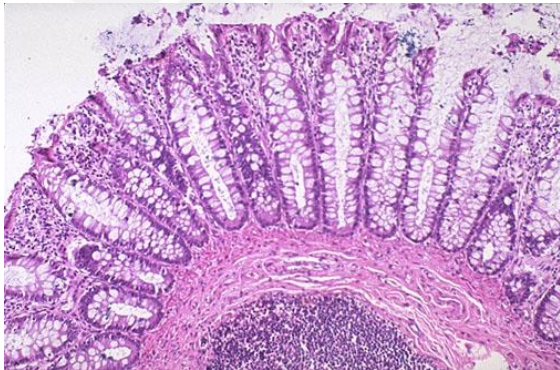
Invasive cancer

Metastatic
cancer

COLON CANCER PROGRESSION



© Mayo Foundation for Medical Education and Research. All rights reserved.



External causes of cancer: ultraviolet radiation



External causes of cancer: tobacco smoke



External causes of cancer:

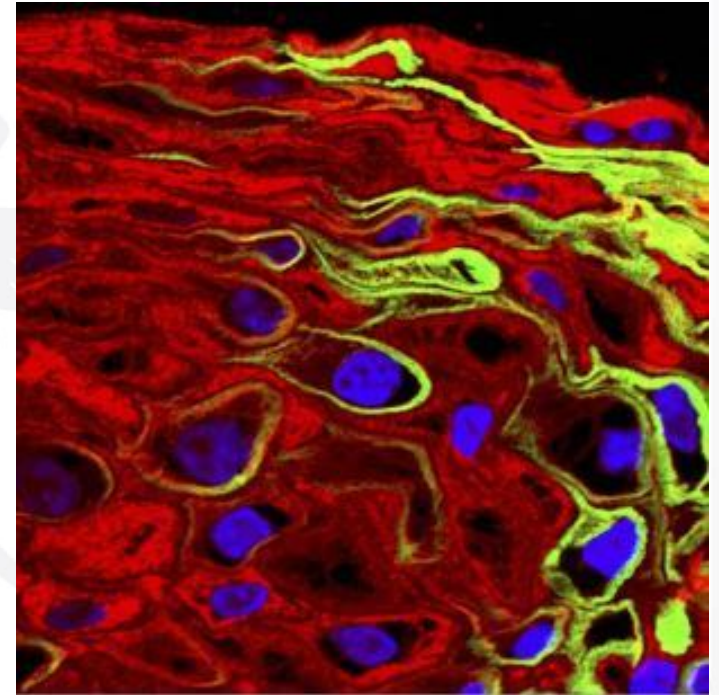
Lifestyle factor: diet



UNIVERSITÀ
DEGLI STUDI
DI PALERMO

Biological factor: virus

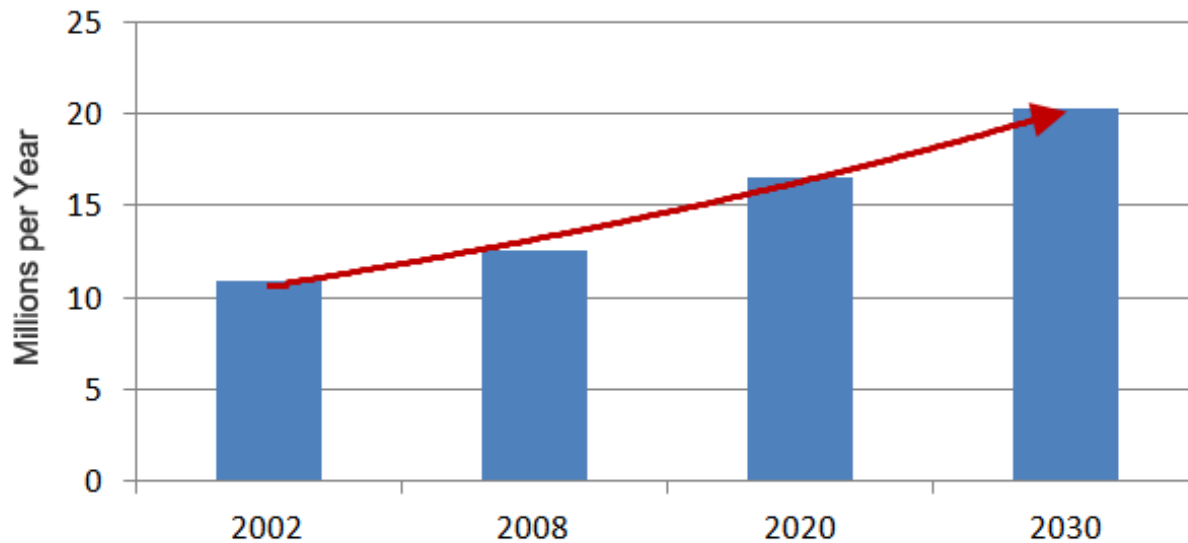
- Human Papilloma Virus is a cause of cervical cancer
- Proteins from the virus activate and deactivate cancer genes
- The role of HPV in cervical cancer has led to the development of vaccines



HPV in cervical epithelium
Credit: MRC NIMR, Wellcome Images

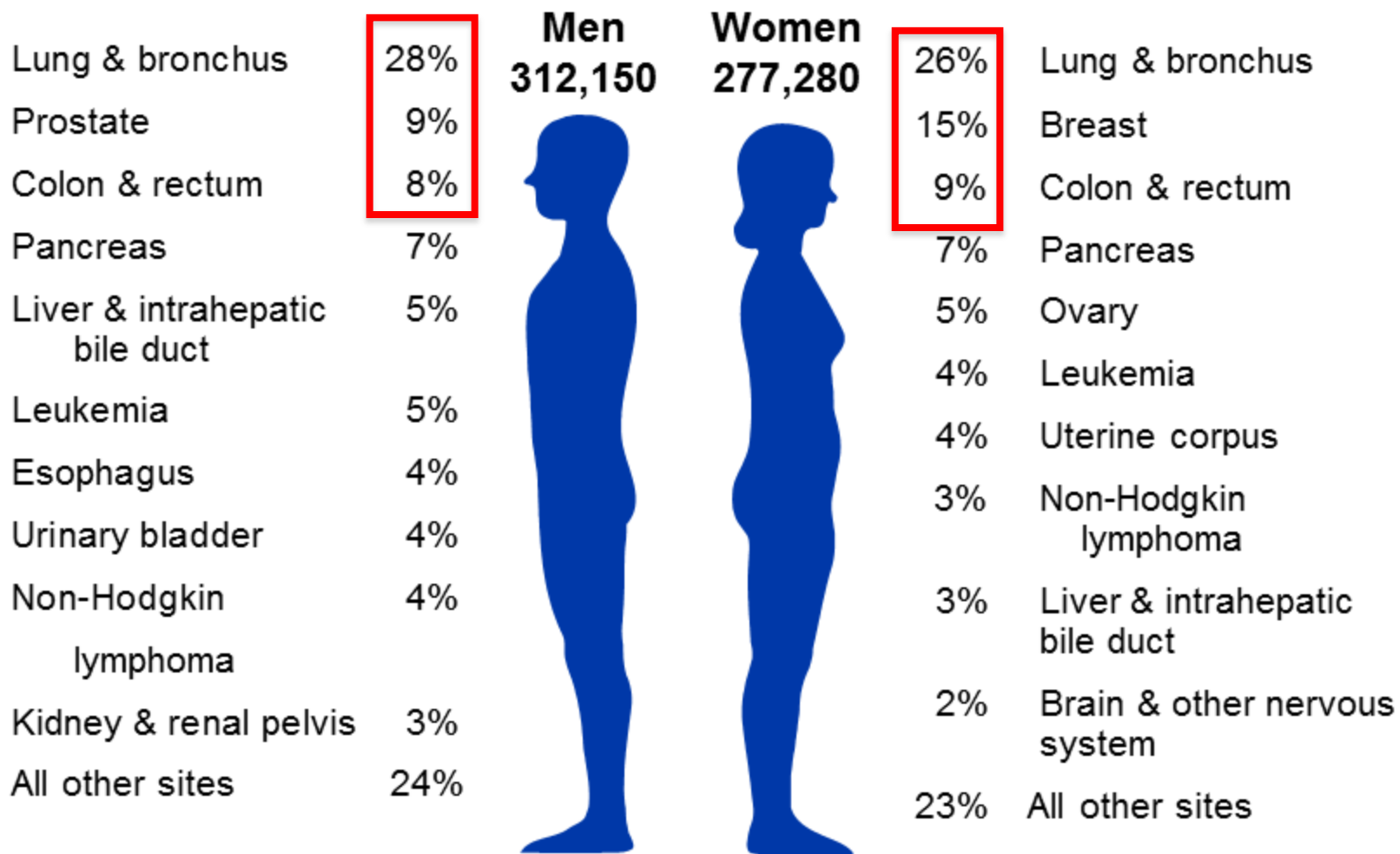
According to World Health Organization, every year more than **10 millions** of people get cancer !!!

Incidence of New Cancers Worldwide Will DOUBLE Between 2002 and 2030



Source: US Center for Disease Control

Estimated Cancer Deaths in the US in 2015



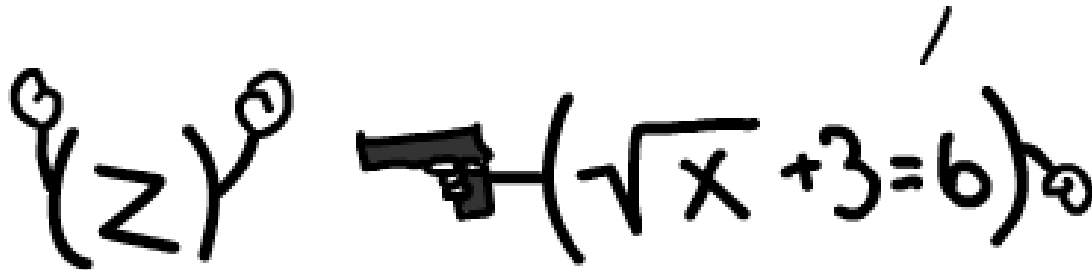
Around 50% of total cancers occur in three organs.....WHY ??????

May foods help to **prevent** Cancer?



What's free radicals ?

I'LL DO IT MAN...I'LL FREAKIN DO IT



**RADICAL EQUATIONS
A DANGER TO SOCIETY**

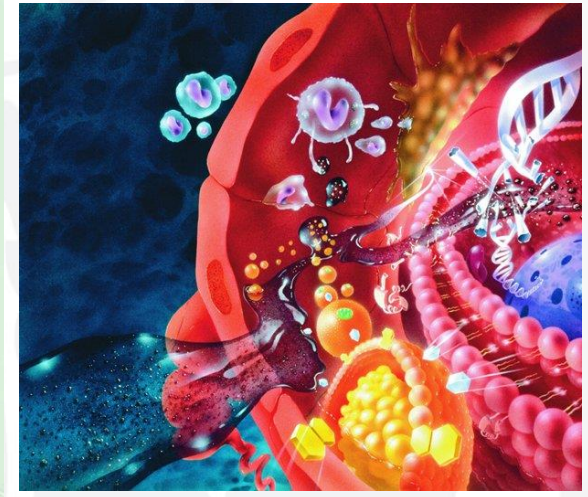
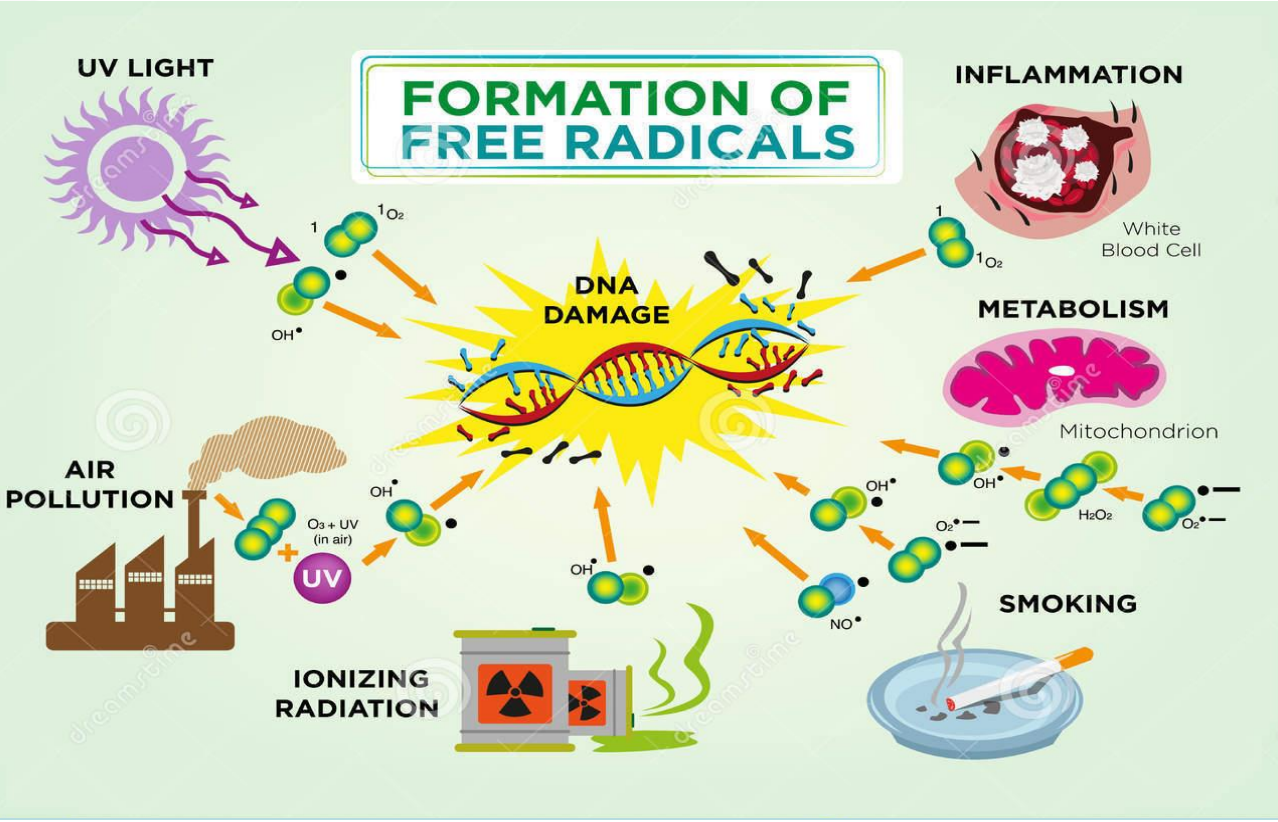
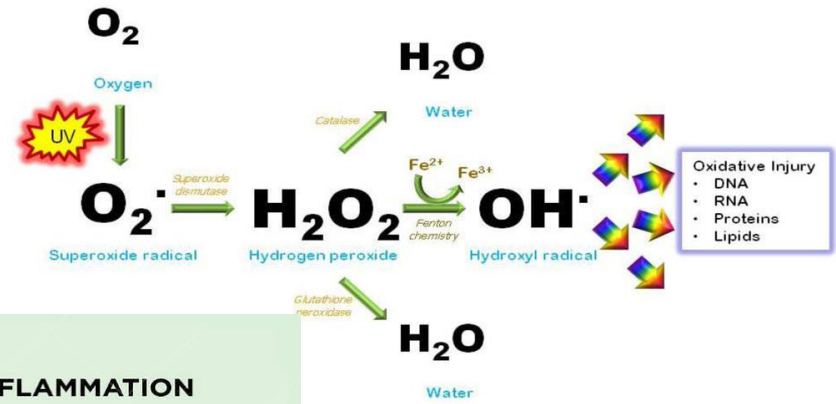
MILDLYHOTPEPPERS.COM - ANTHONY CHEN



UNIVERSITÀ
DEGLI STUDI
DI PALERMO

Whats free radicals ?

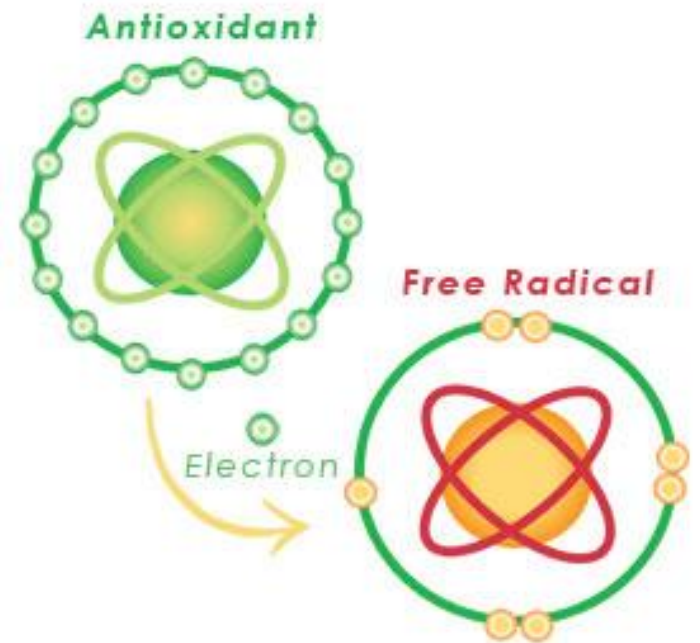
Very unstable compounds



ANTIOXIDANTS



VITAMIN C – VITAMIN E



TRANS-RESVERATROL



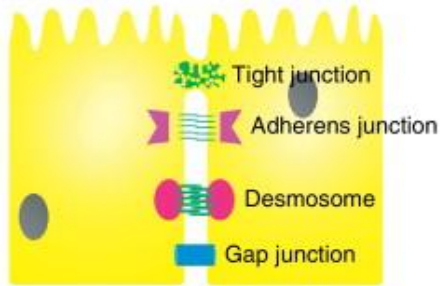
NANOVESICLES IN LEMON JUICE



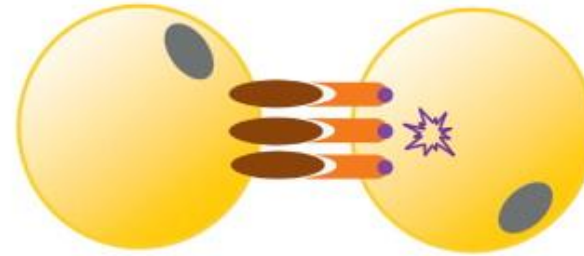
UNIVERSITÀ
DEGLI STUDI
DI PALERMO

CELL-CELL COMMUNICATION

(i) Cell junction



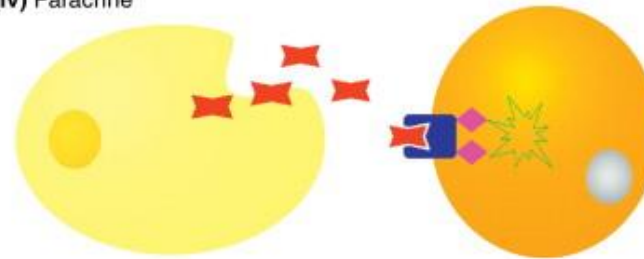
(ii) Adhesion contact



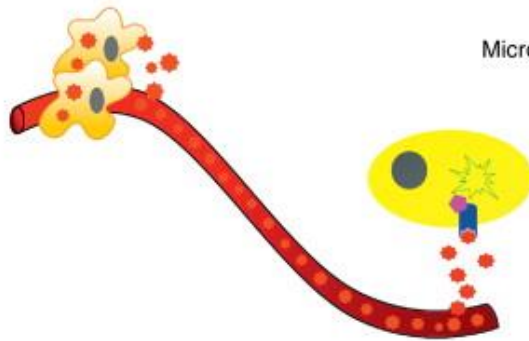
(iii) Autocrine



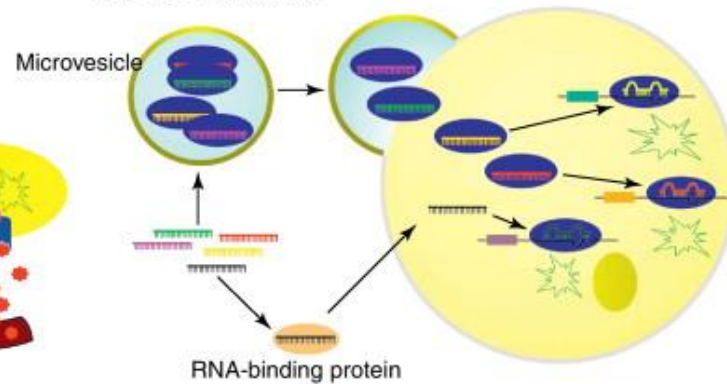
(iv) Paracrine



(v) Endocrine



(vi) Secreted miRNA



TRENDS in Cell Biology



EXOSOMES



Receptor-mediated Endocytosis of Transferrin and Recycling of the Transferrin Receptor in Rat Reticulocytes

CLIFFORD HARDING, JOHN HEUSER, and PHILIP STAHL
*Department of Physiology and Biophysics, Washington University School of Medicine,
St. Louis, Missouri 63110*

Figure 1. **Exocytosis of MVEs releases exosomes containing transferrin receptor.** (left) View of an MVE from a fixed reticulocyte sparsely labeled with AuTf. The apparent fusion of the MVE and the plasma membrane may represent incipient MVE exocytosis. Bar, 100 nm. (right) View of MVE exocytosis in a reticulocyte labeled with AuTf, quick frozen without prior fixation, and freeze substituted. Bar, 200 nm. Figure and legend adapted from Harding et al. (1983).

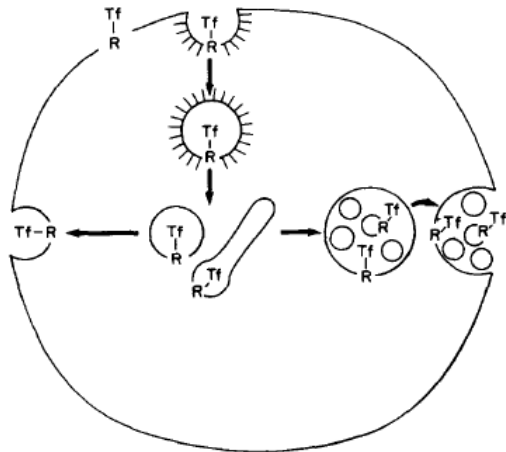
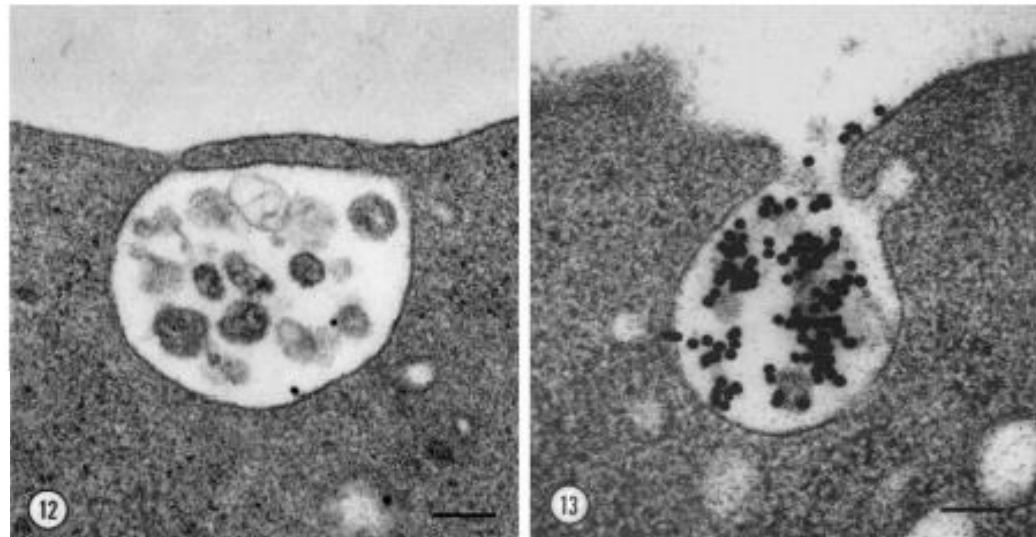
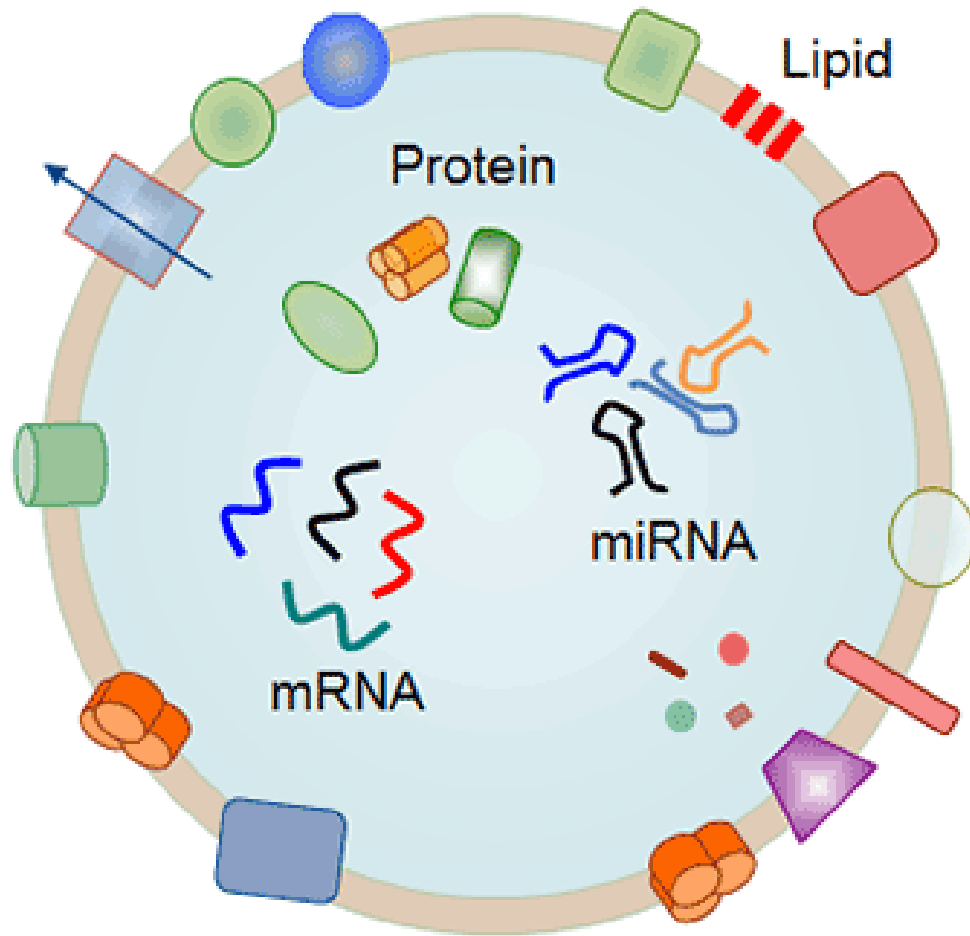
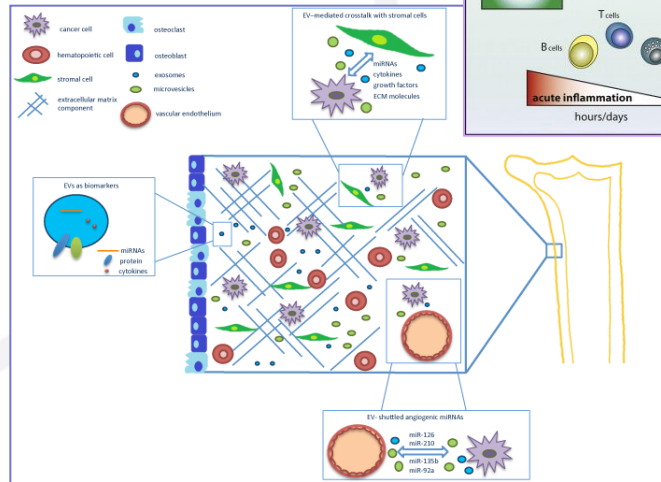
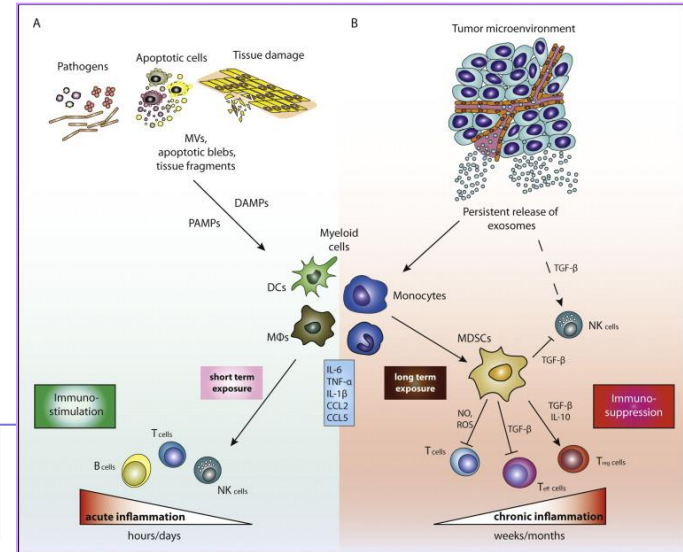


FIGURE 22 Possible routes of transferrin processing in reticulocytes. Transferrin is internalized via coated pits and vesicles. It rapidly appears inside small vesicles and tubules in the reticulocyte cytoplasm; subsequently it is transferred to MVE. Recycling appears to occur from MVE, but transferrin may also recycle directly from small vesicles or tubules to the cell surface.

EXOSOMES ARE CARRIER OF INFORMATION



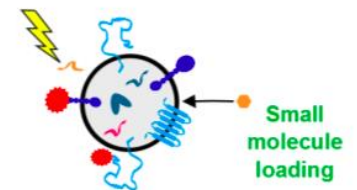
Exosomes in health



Exosomes in disease

Ex vivo Exosome Modification

Introduction of exogenous nucleic acids, e.g. via electroporation



Exosomes as therapeutic agents

NANOVESICLES FROM PLANTS

Grape Exosome-like Nanoparticles Induce Intestinal Stem Cells and Protect Mice From DSS-Induced Colitis



Songwen Ju², Jingyao Mu², Terje Dokland³, Xiaoying Zhuang², Qilong Wang², Hong Jiang², Xiaoyu Xiang², Zhong-Bin Deng², Baomei Wang², Lifeng Zhang², Mary Roth⁵, Ruth Welti⁵, James Mobley⁴, Yan Jun², Donald Miller² and Huang-Ge Zhang^{1,2}

Grapefruit-derived Nanovectors Delivering Therapeutic miR17 Through an Intranasal Route Inhibit Brain Tumor Progression



Xiaoying Zhuang¹, Yun Teng¹, Abhilash Samykutty¹, Jingyao Mu¹, Zhongbin Deng¹, Lifeng Zhang¹, Pengxiao Cao¹, Yuan Rong¹, Jun Yan¹, Donald Miller¹ and Huang-Ge Zhang^{1,2}

NANOVESICLES IN LEMMON JUICE

www.impactjournals.com/oncotarget/

Oncotarget, Advance Publications 2015

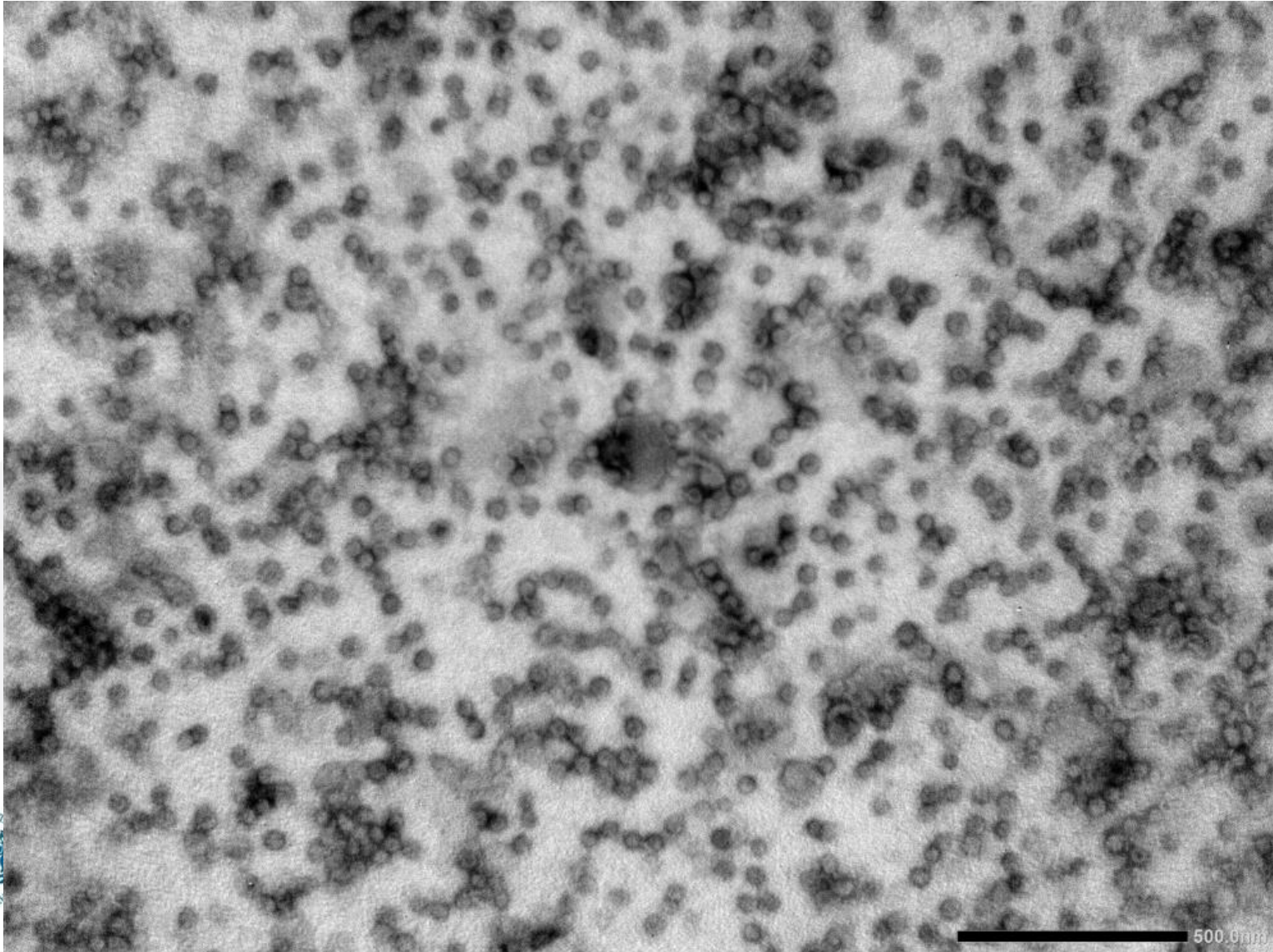
***Citrus limon*-derived nanovesicles inhibit cancer cell proliferation and suppress CML xenograft growth by inducing TRAIL-mediated cell death**

Stefania Raimondo¹, Flores Naselli¹, Simona Fontana¹, Francesca Monteleone¹, Alessia Lo Dico¹, Laura Saieva¹, Giovanni Zito², Anna Flugy¹, Mauro Manno³, Maria Antonietta Di Bella¹, Giacomo De Leo¹, Riccardo Alessandro¹



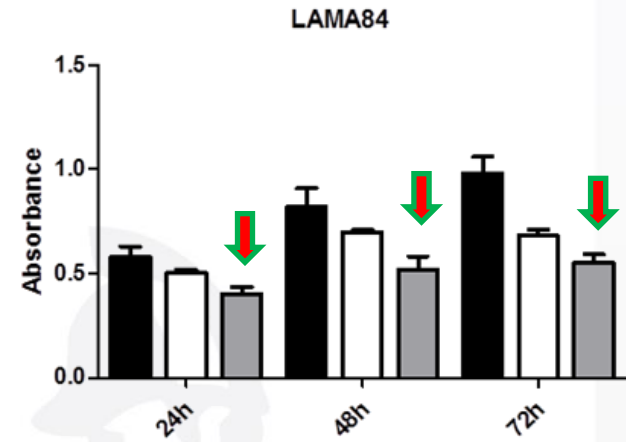
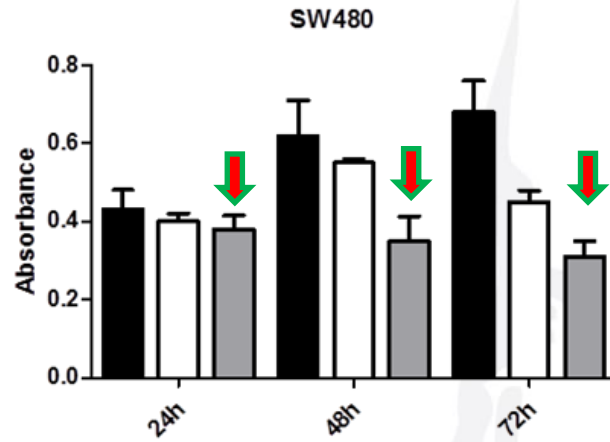
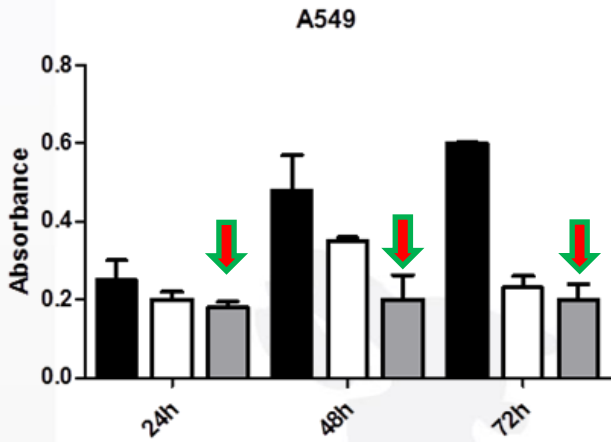
UNIVERSITÀ
DEGLI STUDI
DI PALERMO

Electron Microscope Image of Lemon nanovesicles

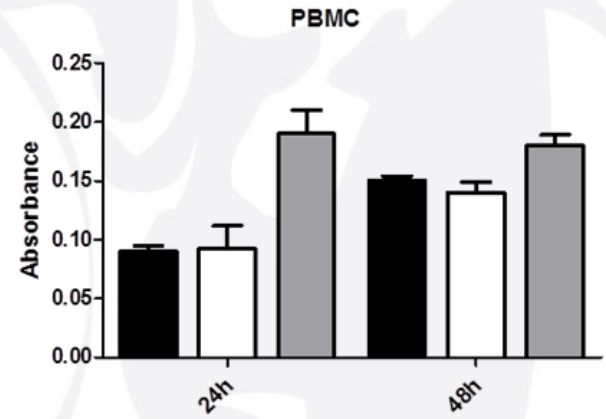
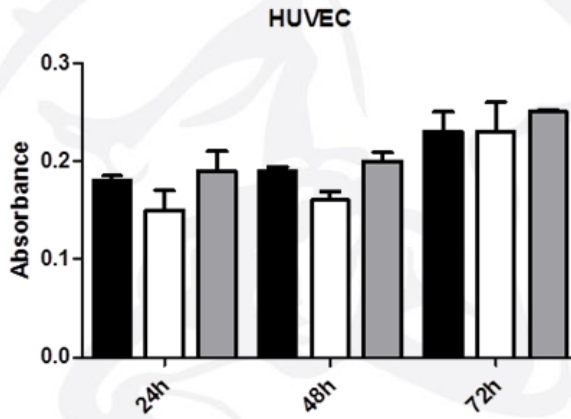
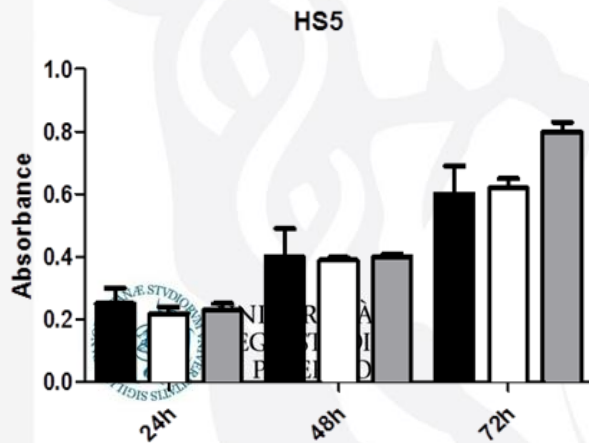


Inhibition of tumor cell growth

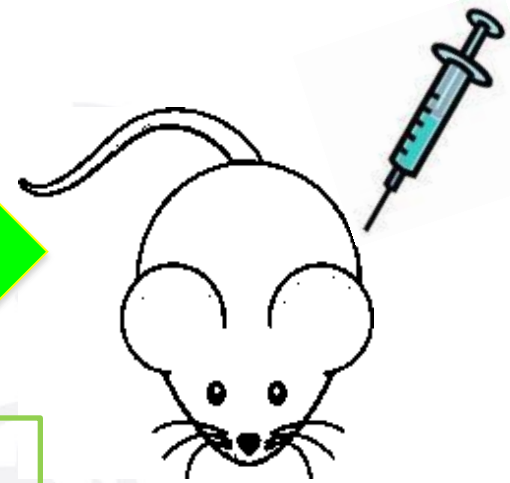
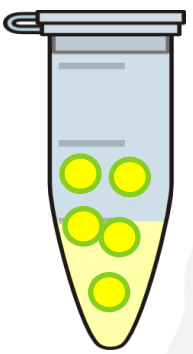
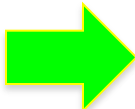
- Ctrl
- nanovesicles 5 $\mu\text{g/ml}$
- nanovesicles 20 $\mu\text{g/ml}$



...but not of normal cells....



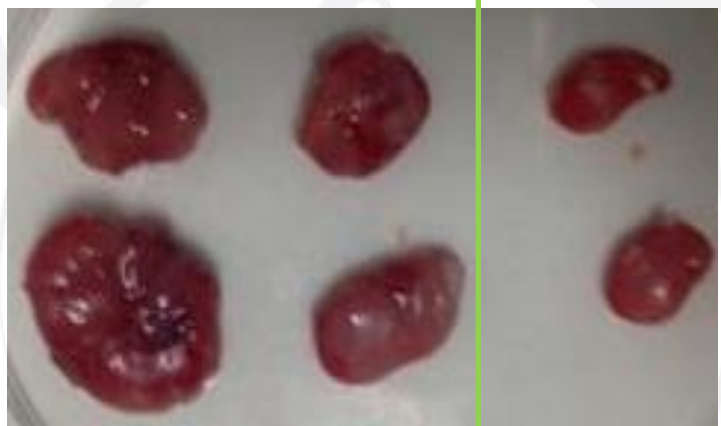
Effect of lemon nanovesicles in a in vivo model of leukemia



Ctrl

Nanoves IT

Nanoves IP



From the laboratory to the business idea





navhetec



UNIVERSITÀ
DEGLI STUDI
DI PALERMO

100% nutraceutical



UNIVERSITÀ
DEGLI STUDI
DI PALERMO





Dipartimento di Biopatologia e
Biotecnologie Mediche



Aroldo Rizzo and Alessandra Santoro



Riccardo Alessandro

Stefania Raimondo
Simona Taverna
Flores Naselli
Alessia Lo Dico
Chiara Corrado
Simona Fontana
Giacomo De Leo

Laura Saieva
Lavinia Raimondi
Angela De Luca
Francesca Monteleone
Daniele Bellavia
Alice Conigliaro
Viviana Costa
Marzia Pucci



Associazione Italiana per la
Ricerca sul Cancro



UNIVERSITÀ
DEGLI STUDI
DI PALERMO

