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Prof. Mauro Ravera

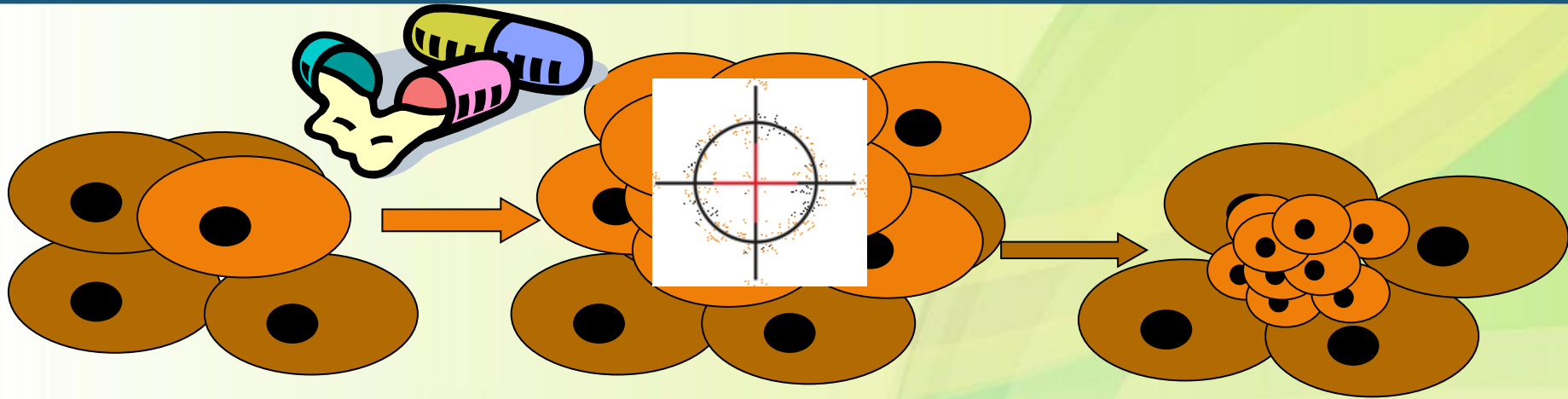
Prof. Domenico Osella

Dipartimento di Scienze ed Innovazione Tecnologica (DiSIT)

Laboratorio di Chimica Bioinorganica e Medica

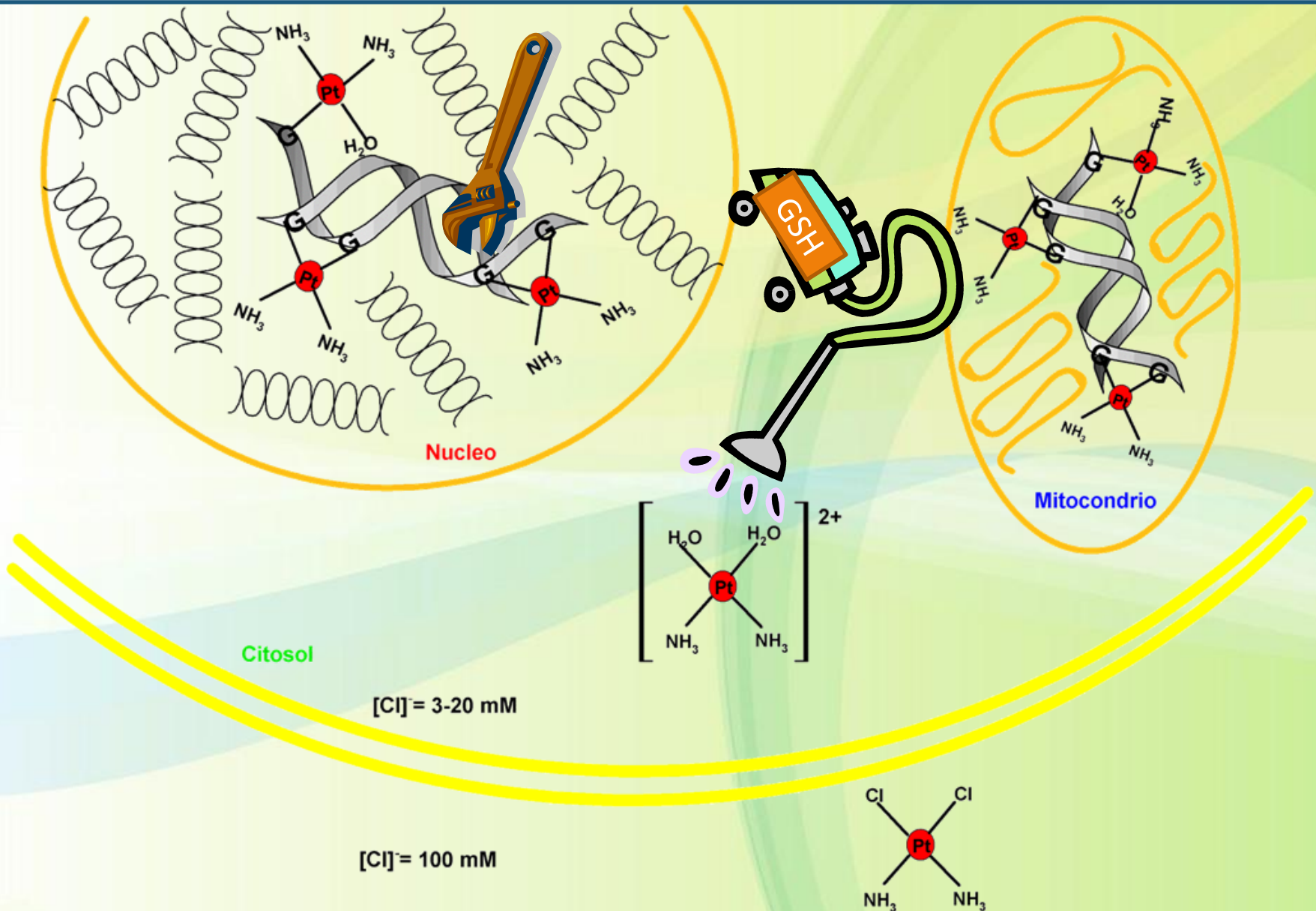
POLICHEMIOTERAPIA DEL MESOTELIOMA BASATA SU COMPLESSI DEL PLATINO

La chemioterapia del mesotelioma

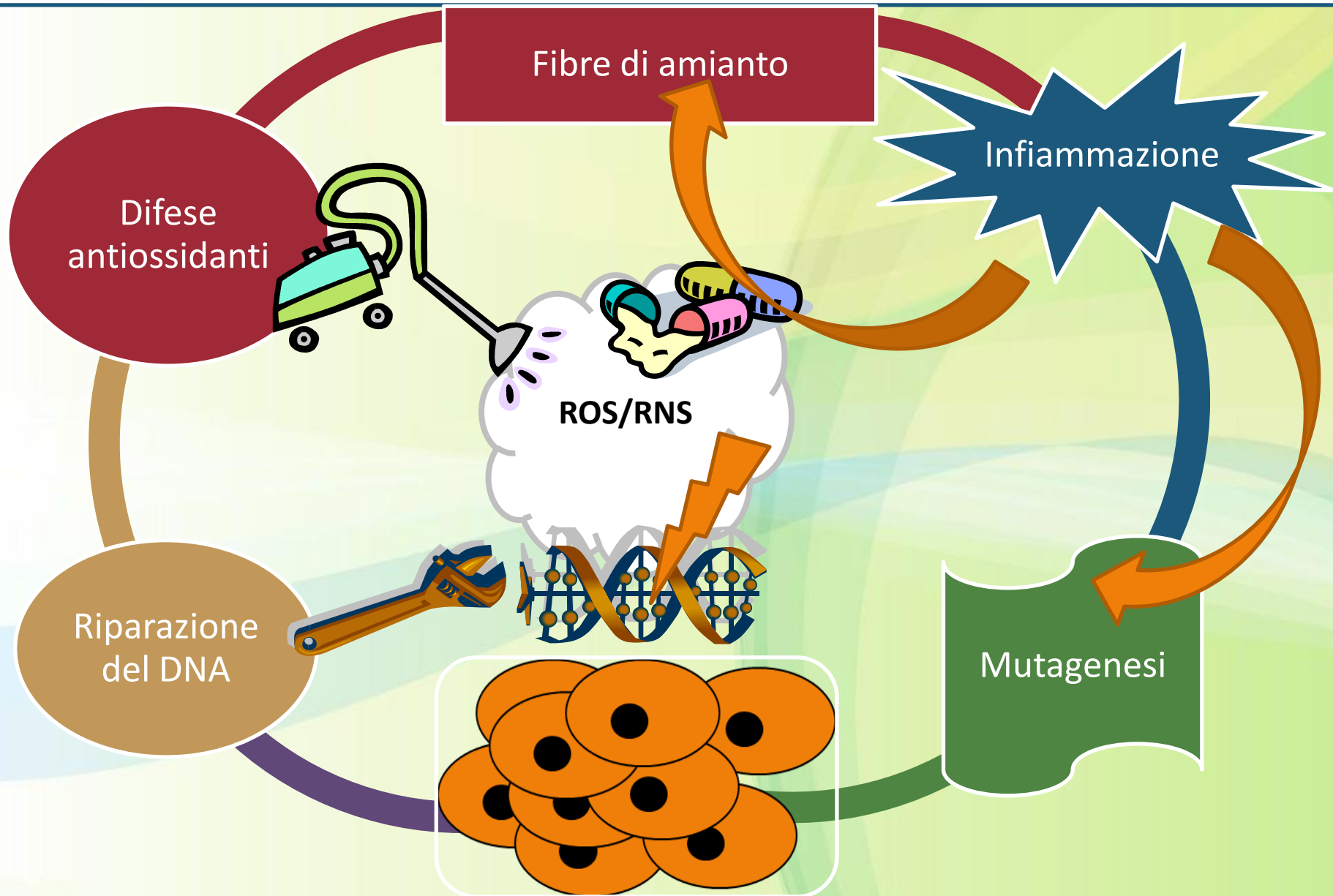


- Basata su un complesso del platino (Pt):
 - Cisplatino/Carboplatino
- In associazione con un farmaco antimetabolita
 - Pemetrexed (antifolato)- Alimta[®]
 - Gemcitabina (analogo delle basi pirimidiniche) Gemzar[®]
- Pesanti effetti collaterali
- Effetto palliativo:
 - Prolunga l'aspettativa di vita
 - Migliora la sintomatologia

Il meccanismo di azione dei complessi a base di Pt



La resistenza innata del mesotelioma



Obiettivi della ricerca *in vitro*

Zanellato I, Bonarrigo I, Gabano E, Ravera M, Margiotta N, Betta P-G, Osella D *Metallo-drugs in the treatment of malignant pleural mesothelioma*. Inorganica Chimica Acta. 393(0):64–74 (2012)

Abbassamento
della resistenza

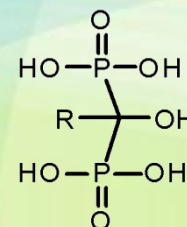
Veicolazione
selettiva

AUMENTO
DELL'EFFICACIA

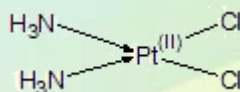
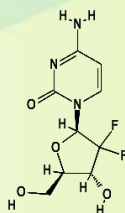


Combinazioni di
farmaci

Bisfosfonati

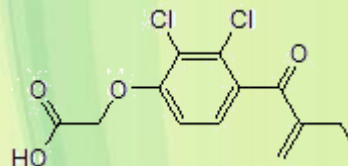


Gemcitabina

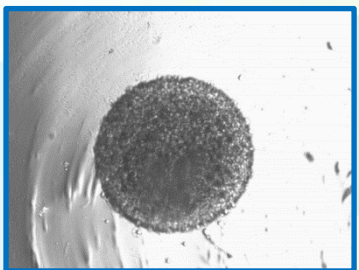
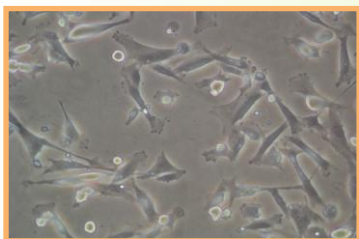
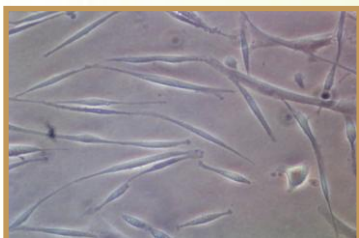
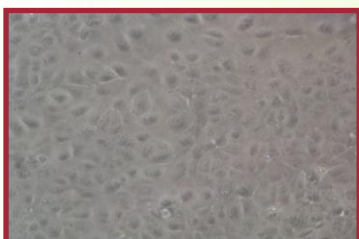
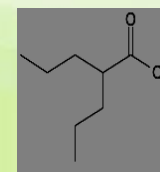


Cisplatino

Acido Etacrinico

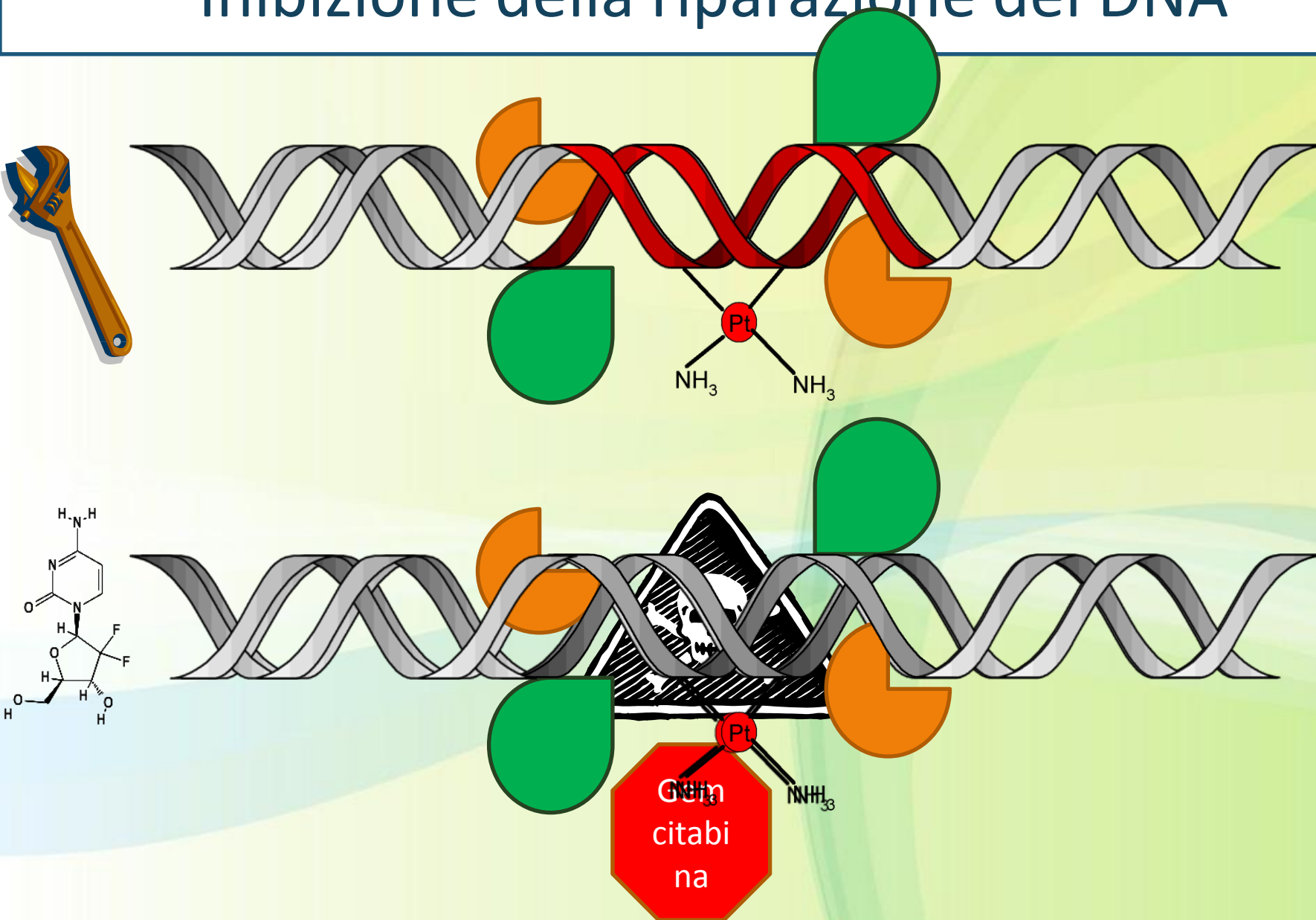


Acido Valproico

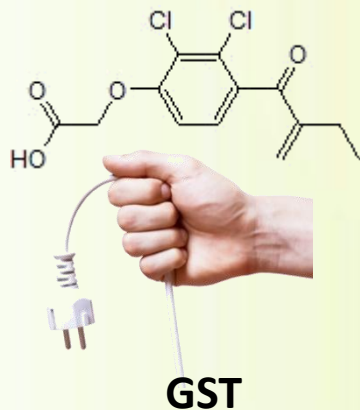


Mesothelioma Biobank Regional Reference Center,
Ospedale di Alessandria

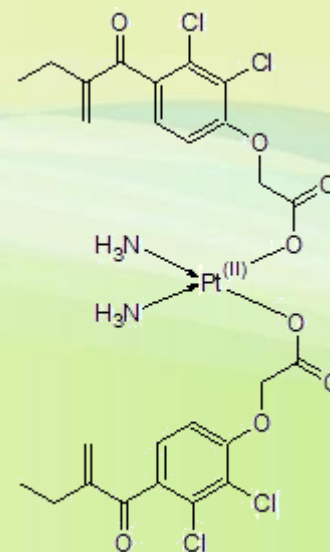
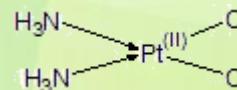
Inibizione della riparazione del DNA



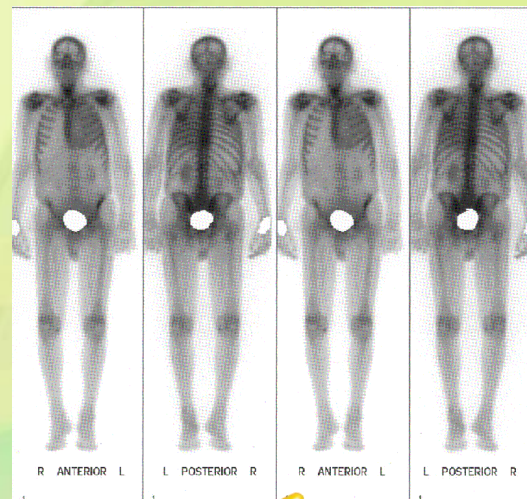
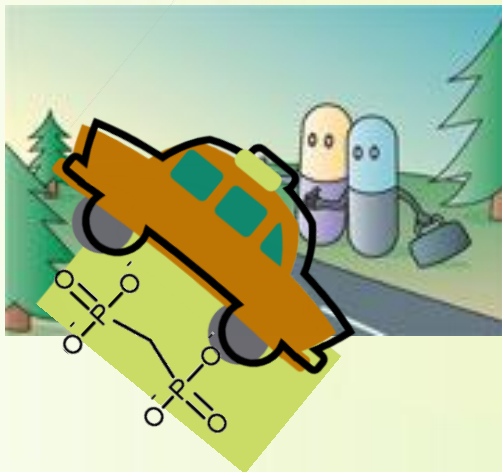
Contrasto alle difese antiossidanti



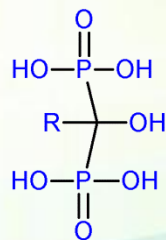
Ravera M, Gabano E, Zanellato I, Bonarrigo I, Escibano E, Moreno V, Font-Bardia M, Calvet T, Osella D. *Synthesis, characterization and antiproliferative activity on mesothelioma cell lines of bis(carboxylato)platinum(IV) complexes based on picoplatin*. Dalton Trans. 41: 3313-3320 (2012)



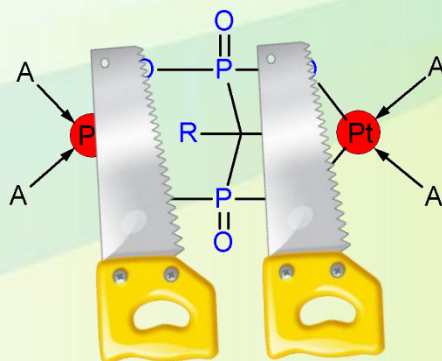
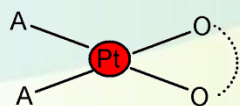
Veicolazione del platino nel mesotelioma



Bisfosfonato



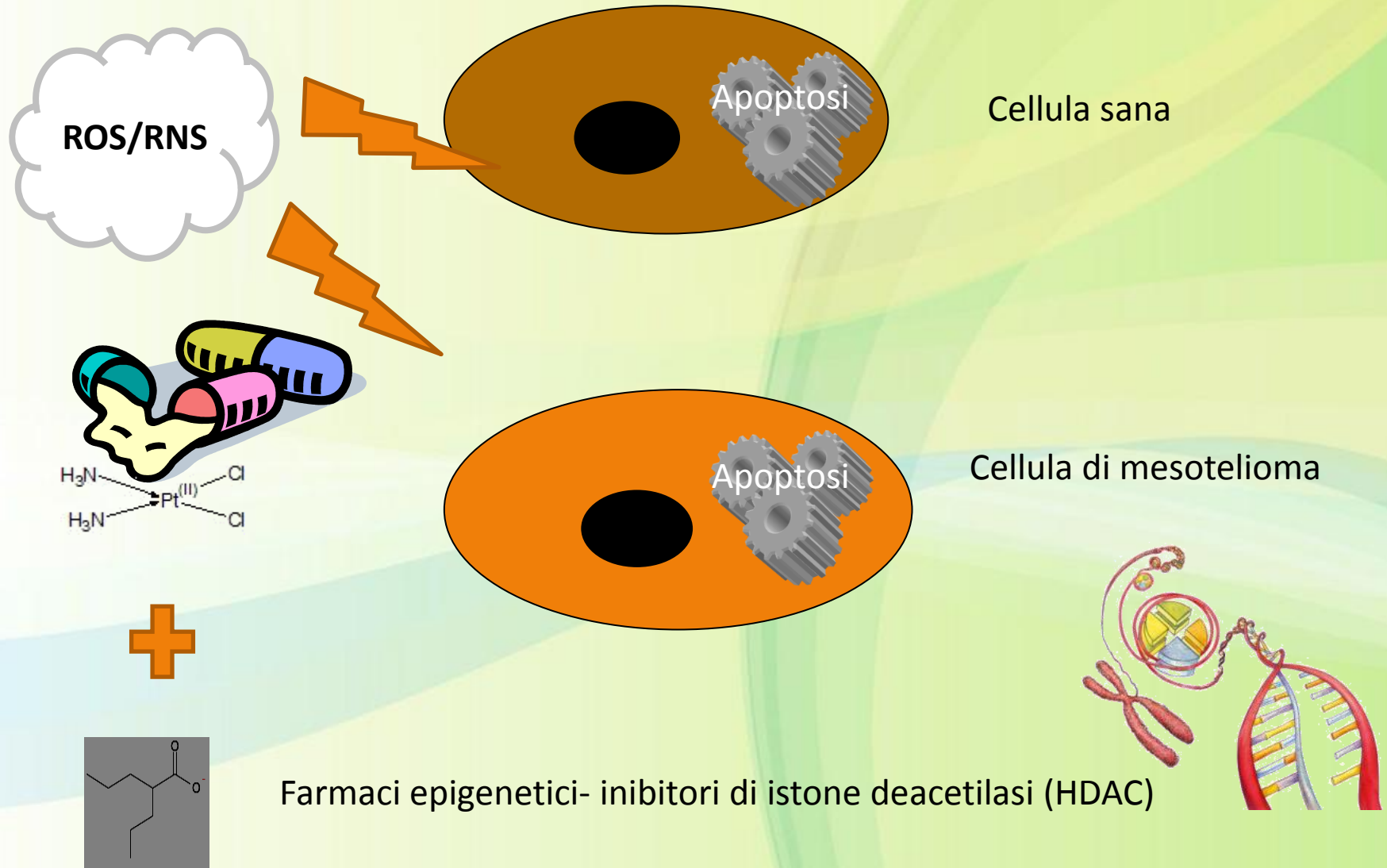
+



Derivato del cisplatino

Margiotta N, Ostuni R, Piccinonna S, Natile G, Zanellato I, Boidi CD, Bonarrigo I, Osella D, *Platinum-bisphosphonate complexes have proven to be inactive chemotherapeutics targeted for malignant mesothelioma because of inappropriate hydrolysis*, Journal of Inorganic Biochemistry, 105, 4: 548-557 (2011)

Abbassamento della resistenza all'apoptosi



Ringraziamenti

- Azienda Ospedaliera SS. Antonio e Biagio e Cesare Arrigo (Alessandria)



FONDAZIONE CRT

- Bando ricerca sanitaria



- Progetto Ricerca Finalizzata CIPE



- Provincia di Alessandria (accordi di programma)



Ministero dell'Istruzione, dell'Università e della Ricerca