

## Mauro Coluccia, Curriculum Vitae



**Mauro Coluccia (21/12/1955)**, Medico-chirurgo, specialista in Oncologia, Professore associato di Patologia generale, è responsabile del laboratorio di Patologia generale, Dipartimento di Farmacia – Scienze del Farmaco dell'Università degli Studi di Bari “Aldo Moro”. Il laboratorio di Patologia generale è attivo nel settore dello sviluppo e delle indagini sul meccanismo d'azione di farmaci antitumorali inorganici, che vengono studiati con tecniche di biologia cellulare e molecolare, con tecnologie genomiche (DNA microarray) e con analisi dell'immagine ad alto

contenuto, al fine di correlare le caratteristiche strutturali di farmaci in uso e di candidati farmaci con i geni e prodotti genici che guidano la risposta cellulare al trattamento. Di maggiore interesse è il fatto che vengono utilizzati modelli sperimentali clinicamente rilevanti: in particolare, cellule tumorali e altre cellule del microambiente provenienti da pazienti affetti da tumore.

I principali risultati ottenuti hanno riguardato la scoperta di una nuova classe di complessi antitumorali di platino a geometria “trans”, e il contributo al chiarimento del meccanismo d'azione di un nuovo complesso di rutenio denominato NAMI-A. Complessivamente, i lavori scientifici su diversi complessi antitumorali inorganici -pubblicati su importanti riviste internazionali- sono stati citati più di 2000 volte (SCOPUS). Per quanto riguarda i complessi di platino a geometria trans, la loro scoperta ha determinato un importante avanzamento delle conoscenze su questa classe di farmaci, e i lavori scientifici sull'argomento sono stati citati oltre 1000 volte (SCOPUS), e uno di essi risulta al primo posto della lista dei “top 20 article in the domain since its publication in 2004” (MioMedLib WIPIMD). Il lavoro sui complessi di rutenio ha contribuito al chiarimento della loro modalità di interazione con il DNA, e ha condotto alla scoperta dell'attività anti-angiogenica del NAMI-A, attualmente in fase di sperimentazione clinica; i lavori sull'argomento sono stati citati oltre 250 volte (SCOPUS).

### PARTECIPAZIONE A PROGETTI DI RICERCA NAZIONALI E INTERNAZIONALI

-Responsabile scientifico di Unità Operativa, Progetto finalizzato CNR “Applicazioni cliniche della ricerca oncologica” (1993-1996)

-Principal Investigator nel Progetto Europeo Biomed BMH4-97-2485 “Modulation of gene expression by platinated oligonucleotides”.

-Coordinatore del Progetto Europeo “The development of antitumour platinum complexes with trans geometry” (COST/D8/0007/97)

- Responsabile scientifico dell'Unità Operativa “Chemioterapia sperimentale” nell'ambito del progetto: Farmacoprevenzione nei pazienti con mieloma multiplo. Inibizione dell'angiogenesi e della crescita tumorale con inibitori delle COX-2, Ministero della Salute, Progetti Strategici di Area Biomedica (2003-2005).

- Responsabile scientifico dell'Unità Operativa “Sviluppo farmacologico di complessi antitumorali di platino con imminoeteri e con ditiocarbammati”, nell'ambito del progetto: Controllo della proliferazione, della

motilità e dell'invasione tumorale: sviluppo farmacologico di nuovi antitumorali a base metallica, PRIN 2004.

- Responsabile scientifico dell'Unità Operativa "Sintesi, screening e studi meccanicistici di complessi antitumorali metallo-peptide", nell'ambito del progetto: Delivery selettivo di complessi metallici farmacologicamente attivi mediante sonde peptidiche e nano sistemi funzionalizzati con peptidi bioattivi (PRIN2009).

- Responsabile scientifico dell'Unità Operativa "Nuovi derivati di platino e Rutenio e loro utilizzazione nelle neoplasie chemioresistenti" nell'ambito del Progetto Strategico Regione Puglia - APQ "Le Biotecnologie applicabili alla targeted therapy in oncologia (Biotecnoter)" (2010-2012).

- Partecipante al progetto "Overcoming clinical relapse in multiple myeloma by understanding and targeting the moleculare causes of drug resistance (OVER-MyR), EU FP7-Health, 2011.

### **PUBBLICAZIONI SCIENTIFICHE**

M.Coluccia è autore o co-autore di 68 lavori su riviste internazionali (9 capitoli su libri), e co-inventore di brevetti industriali internazionali.

1. COLUCCIA M, CORREALE M, FUMARULO R, GIORDANO D (1983). Ulteriori contributi allo studio dell'interazione cisplatino-DNA. FOLIA ONCOLOGICA, vol. 6, p. 264-272, ISSN: 0392-047X.

2. ARESTA M, TREGLIA S, COLUCCIA M, CORREALE M, GIORDANO D, MOSCELLI S (1984). Mutagenic activity of transition metal complexes: relation structure-mutagenic and antibacterial activity for some Pd(II), Pt(II) and Rh(I) complexes. TOXICOLOGICAL AND ENVIRONMENTAL CHEMISTRY, vol. 8, p. 81-94, ISSN: 0277-2248.

3. COLUCCIA M, CORREALE M, FANIZZI FP, GIORDANO G, MARESCA L, MARIGGI MA, NATILE G, TAMARO M (1984). Mutagenic activity of some paltinum complexes: Chemical properties and biological activity. TOXICOLOGICAL AND ENVIRONMENTAL CHEMISTRY, vol. 8, p. 1-8, ISSN: 0277-2248.

4. FUMARULO R, RICCARDI S, PANTALEO R, COLUCCIA M, GIORDANO D, ARESTA M. (1985). In vitro cisplatin effects on phagocyte functions. INTERNATIONAL JOURNAL OF CANCER, vol. 35, ISSN: 0020-7136.

5. COLUCCIA M, CORREALE M, FANIZZI FP, GIORDANO D, MARESCA L, MARIGGIO MA, NATILE G, TAMARO M (1985). Mutagenic activity of some platinum complexes: chemical properties and biological activity. In: MERIAN E, FREI RW, HARDI W, SCHLATTER C. CARCINOGENIC AND MUTAGENIC METAL COMPOUNDS. pp. 467-474, NEW YORK:Gordon & Breach Sci Publ.

6. ARESTA M, TREGLIA S, COLUCCIA M, CORREALE M, GIORDANO D, MOSCELLI S (1985). Mutagenic activity of transition metal complexes: relation structure-mutagenic and antibacterial activity for some Pd(II), Pt(II) and Rh(I) complexes. In: MERIAN E, FREI RW, HARDI W, SCHLATTER C. (eds), CARCINOGENIC AND MUTAGENIC METAL COMPOUNDS. pp. 453-466, NEW YORK:Gordon & Breach Sci Publ.

7. COLUCCIA M, CORREALE M, GIORDANO D, MARIGGO MA, MOSCELLI S, FANIZZI FP, NATILE G, MARESCA L (1986). Mutagenic activity of some platinum complexes with monodentate and bidentate amines. INORGANICA CHIMICA ACTA, vol. 123, p. 225-229, ISSN: 0020-1693.

8. FANIZZI FP, INTINI FP, MARESCA L, NATILE G, QUARANTA R, COLUCCIA M, DIBARI L, GIORDANO D, MARIGGI MA (1987). Biological activity of platinum complexes containing chiral centers on the nitrogen or carbon atoms of a chelate diamine ring. *INORGANICA CHIMICA ACTA*, vol. 137, p. 45-51, ISSN: 0020-1693.
9. MONTEMURRO P, COLUCCIA M, DE NICOLO L, COLUCCI M, SEMERARO N. (1988). Treatment with cyclosporin A does not affect macrophage procoagulant activity and plasminogen activator inhibitor in mice. *PHARMACOLOGICAL RESEARCH COMMUNICATIONS*, vol. 20, ISSN: 0031-6989.
10. FUMARULO R, RICCARDI S, FIORE A, COLUCCIA M (1988). Modifications of phagocyte functions in macrophages from Cyclosporin A-treated mice. *LIFE SCIENCE ADVANCES BIOCHEMISTRY*, vol. 7, p. 199-200, ISSN: 0971-510X.
11. COLUCCIA M, GIORDANO D, LOSETO F, INTINI FP, MARESCA L, NATILE G. (1989). Different binding to DNA of enantiomeric platinum complexes assessed by inhibition of restriction enzyme activity. *ANTICANCER RESEARCH*, vol. 9, ISSN: 0250-7005.
12. COLUCCIA M, FANIZZI FP, GIANNINI G, GIORDANO D, INTINI FP, LACIDOGNA G, LOSETO F, MARIGGIO MA, NASSI A, NATILE G. (1991). Synthesis, mutagenicity, binding to pBR 322 DNA and antitumour activity of platinum(II) complexes with ethambutol. *ANTICANCER RESEARCH*, vol. 11, ISSN: 0250-7005.
13. LOSETO F, ALESSIO E, MESTRONI G, LACIDOGNA G, NASSI A, GIORDANO D, COLUCCIA M (1991). Interaction of RuCl<sub>2</sub> (dimethylsulphoxide)<sub>4</sub> isomers with DNA. *ANTICANCER RESEARCH*, vol. 11, ISSN: 0250-7005.
14. COLUCCI M, COLUCCIA M, MONTEMURRO P, CONESE M, NASSI A, LOSETO F, ALESSIO E, MESTRONI G, SEMERARO N (1993). reduction of tumor-associated fibrinolytic activity by antimetastatic dosages of two Ru(II)-DMSO complexes in mice bearing lewis lung carcinoma. *INTERNATIONAL JOURNAL OF ONCOLOGY*, vol. 2, p. 527-529, IS6 1993
15. MESTRONI G, ALESSIO E, SAVA G, PACOR S, COLUCCIA M (1993). The development of tumor-inhibiting ruthenium dimethylsulfoxide complexes. In: KEPLER BK. *METAL COMPLEXES IN CANCER CHEMOTHERAPY*. p. 157-185, WEINHEIM:VCH.ISSN: 1019-6439.
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35. A. BOCCARELLI, COLUCCIA M, F.P. INTINI, G. NATILE, D. LOCKER, M. LENG (1999). Cytotoxicity and DNA binding mode of new platinum iminoether derivatives with different configuration at the iminoether ligands. ANTI-CANCER DRUG DESIGN, vol. 14, ISSN: 0266-9536.

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#### **BREVETTI INDUSTRIALI**

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2. F.P. INTINI, G. NATILE, A. BOCCARELLI, COLUCCIA M (2002). Method for synthesizing complexes of platinum with iminoethers and their use as antitumoral drugs and nucleotide base modifiers. United States Patent 6458983, Università di Bari.

#### **ALTRE ATTIVITÀ SCIENTIFICHE**

M. Coluccia è *Editor* delle riviste *Metal-Based Drugs*, *Journal of Pharmaceutics & Drug Development*, *International Journal of Molecular Sciences*, e svolge attività di *referee* sia per numerose riviste scientifiche (*Int J Cancer*, *Biochem Pharmacol*, *J Med Chem*, *Br J Cancer*, *Mol Pharmaceutics*, *Crit Rev Hematol Oncol*, *J Inorg Biochem*, *Eur J Pharm Sci*) sia per Agenzie di finanziamento internazionali (*Austrian Science Fund*; *Science and Technology Foundation of Portugal*; *Grant Agency of the Czech Republic*; *Wellcome Trust, UK*); ha curato l'edizione italiana del trattato "*Robbins Basic Pathology Ninth Edition*", Elsevier Saunders, Philadelphia, 2013.

#### **CONFERENZE/CONGRESSI**

M. Coluccia è stato invitato a tenere conferenze e/o in qualità di Chairman in numerosi Congressi Nazionali e Internazionali, alcuni dei quali sono di seguito elencati.

- **3rd International Conference of Anticancer Research**, Marathon, Greece, 1990. **Lecture:** Relevance of mutagenicity and DNA interaction tests in antitumor activity studies.

- **Seminari scientifici Fondazione CD Callerio:** Meccanismi di attività antitumorale di composti di rutenio, Trieste 1992. **Lecture:** DNA interactions and antileukemic activity.

- **HCM Meeting: Studies towards new platinum drugs**, Paris 1993. **Lecture:** Platinum-iminoether complexes as non-classical cisplatin analogues.



- **CERC3 Workshop on Coordination chemistry in the context of biological and environmental studies**, Toulouse 1994. **Lecture:** Mechanistic studies on anticancer platinum iminoether complexes.
- **2<sup>nd</sup> Workshop on Biocoordination chemistry**, Copenhagen 1996. **Lecture:** Trans platinum complexes with antitumor activity.
- **Coordination chemistry in the context of biological and environmental studies**, Bergen 1997. **Lecture:** Cellular and biochemical properties of antitumor trans platinum iminoether complexes.
- **Biomed 2 Meeting: Modulation of gene expression by platinated nucleotides**, Bergen 1997. **Lecture:** Platinum iminoether complexes as cross-linking agents.
- **Workshop on Chelators and metal-macromolecule interactions in medicine**, Session "The development of antitumor platinum complexes with trans geometry, Windsor 1997 (**Chairman**).
- **COST D8: The development of antitumor platinum complexes with trans geometry**, Madrid 1998. **Lecture:** Antitumor activity of platinum iminoether complexes.
- **Workshop on Chemistry of metals in medicine**, Ivrea 1998. **Lecture:** Antiangiogenic activity of the ruthenium complex trans-RuCl<sub>4</sub>DMSOIm.
- **Workshop on Chemistry of metals in medicine**, Oxford 1999 (**Chairman**).
- **8<sup>th</sup> International Symposium on platinum and other metal coordination compounds in cancer chemotherapy**, Oxford 1999. **Lecture:** Synthesis and in vitro and in vivo activity of new platinum iminoether derivatives with different configurations at the iminoether ligands.
- **International conference on DNA conformation, modification and recognition in Biomedicine**, Brno 2000 (**Chairman**).
- **International conference on DNA conformation, modification and recognition in Biomedicine**, Brno 2000. **Lecture:** Antitumor transplatinum derivatives.
- **5<sup>th</sup> European biological inorganic chemistry conference**, Toulouse 2000. **Lecture:** The development of antitumor trans platinum iminoether derivatives.
- **COST D8 Final workshop on the Chemistry of metals in medicine**, Dublin 2001. **Lecture:** The development of antitumor compounds with trans geometry.
- **26<sup>mo</sup> Congresso Nazionale SIP**, Catania 2002. Analisi dell'espressione genica (DNA microarray) in cellule endoteliali e cellule tumorali dopo trattamento con il farmaco antimetastatico sperimentale NAMI-A.
- **1<sup>st</sup> International conference on cancer therapeutics, molecular targets, pharmacology and clinical applications**, Firenze 2004. **Lecture:** Antitumor platinum iminoether complexes.
- **COST D20 Biochemistry, structural and cellular biology of non-classical antitumor platinum compounds**, Jerusalem 2005. **Lecture:** Identification of genes associated with platinum iminoether compounds activity in ovarian cancer cells.
- **COST D20 Biochemistry, structural and cellular biology of non-classical antitumor platinum compounds**, Jerusalem 2005 (**chairman**).

- **28mo Congresso nazionale SIP 2006**, Pavia 2006. Inibizione di metalloproteasi da parte di complessi di platino con bisfosfonati.
- **Israel Science Foundation Workshop on Metal containing anticancer agents. Jerusalem 2007** (Chairman)
- **29mo Congresso nazionale SIP 2008. Rende Cosenza 2008.** Zoledronic acid affects the angiogenic phenotype of bone marrow endothelial cells in multiple myeloma patients.
- **11<sup>th</sup> workshop on Pharmacobiometallics 2011**, San Benedetto 2011. **Lecture:** Screening tests for selecting anticancer metal compounds.