Università degli Studi di Roma "Tor Vergata"

CURRICULUM DIDATTICO-SCIENTIFICO DELLA PROF.SSA ANNA MARIA CACCURI

DATI PERSONALI
Nome e Cognome: ANNA MARIA CACCURI
Luogo e data di nascita: ROMA, 28.10.1955

***ATTUALE POSIZIONE*:** Professore Associato di Biochimica
Dipartimento: Medicina Sperimentale e Chirurgia
Indirizzo: Università di Roma "Tor Vergata" via Montpellier 1 - 00133 ROMA
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Orario ricevimento: da concordare
Settore scientifico-disciplinare: BIO/10 - BIOCHIMICA

ATTIVITA' DIDATTICA - SCIENTIFICA

Titoli accademici e di studio:
1979 - Laurea in Scienze Biologiche (cum laude) Università di Roma "La Sapienza".
1983 – Ricercatore presso l'Università di Chieti "G. D'Annunzio".
1986-2001 Ricercatore presso l'Università di Roma "Tor Vergata".
2001-2018 Professore Associato presso l'Università di Roma "Tor Vergata".

Formazione post-laurea presso istituzioni italiane ed estere ed incarichi professionali (didattici e di ricerca):
Dal 1987 al 1988 ha svolto attività di ricerca all'estero come Post-doc fellow presso
1) il laboratorio diretto dal Prof. Yogesh C. Awasthi dell'Università del Texas di Galveston (Dipartimento di Genetica e Chimica Biologica Umana)
2) il laboratorio diretto dal Prof. John K. Heath dell'Università di Oxford (Dipartimento di Biochimica)

Finanziamenti e premi ricevuti per attività di ricerca:
2005: contratto di ricerca: "study of the interaction between the enzyme glutathione S-transferase detoxifying skin and the substances listed in the CE / 39/2000 with the notation 'skin 'aimed at biological monitoring of exposed subjects" finanziato da ISPESL (Ruolo: PI).
2007-2010 progetto: "Alliance Against Cancer" finanziato da ISS (Ruolo: responsabile unità di ricerca).
2008 contratto di ricerca " Identification of Molecular Markers for the development of new diagnostic and therapeutic strategies in the treatment of Mesothelioma" finanziato da ISPESL (Ruolo: PI).
2010-2013 progetto: "Exploiting the protein-protein interaction properties of glutathione transferase GSTP1-1 for cancer treatment" finanziato da AIRC (Ruolo: PI).
2016-2017 progetto: "Role of the glutathione transferase inhibitor MC3181 in the modulation of the growth and metastatic spreading of cutaneous melanoma" finanziato dall'Università di Roma "Tor Vergata" fondi: "CONSOLIDATE THE FOUNDATIONS" (Ruolo: PI).
2016-2018 progetto: "Studio del potenziale ruolo protettivo dell'enzima glutatione trasferasi nei confronti di fattori che inducono neurodegenerazione retinica.

Analisi dell'effetto della variabilità glicemica su cellule gliali retiniche" finanziato dal Ministero della salute (5x1000) e dalla Fondazione Roma (Ruolo PI).

Attività di ricerca: 15 pubblicazioni selezionate

Nel 2002, Anna Maria Caccuri ha dato inizio ad un filone di ricerca che ha portato alla sintesi di una nuova classe di potenti inibitori delle glutatione trasferasi. I composti presentano un meccanismo d'azione unico e proprietà antitumorali promettenti. I composti sono inclusi nel brevetto statunitense (US 8,796,317 B2 del 05/08/2014 (USE OF 7-NITRO-2,1,3-BENZOXADIAZOLE DERIVATIVES FOR ANTICANCER THERAPY, Caccuri et al.) e in quello italiano No 0001412189 (DERIVATI DEL 7-NITRO-2,1,3-BENZOSSADIAZOLO PER TERAPIA ANTITUMORALE, Mai, Caccuri et al). In particolare, il composto MC3181 risulta essere altamente efficace contro cellule di melanoma umano con mutazione BRAFV600E, sia sensibili che resistenti al farmaco vemurafenib.

1. The nitrobenzoxadiazole derivative MC3181 blocks melanoma invasion and metastasis. De Luca A. et al. **Oncotarget. 2017;8(9):15520-15538.**
2. New insight into the interaction of TRAF2 C-terminal domain with lipid raft microdomains. Ceccarelli A. et al. **Biochim Biophys Acta. 2017;1862(9):813-822.**
3. A new water soluble MAPK activator exerts antitumor activity in melanoma cells resistant to the BRAF inhibitor vemurafenib. Graziani G. et al **Biochem Pharmacol. 2015;95(1):16-27.**
4. A Novel Orally Active Water-soluble Inhibitor of Human Glutathione Transferase Exerts a Potent and Selective Antitumor Activity against Human Melanoma Xenografts. De Luca A. et al . **Oncotarget. 2015;6(6):4126-43.**
5. Synthesis and structure-activity relationship of new cytotoxic agents targeting human glutathione-S-transferases. Rotili D. et al. **Eur J Med Chem. 2015;89:156-71.**
6. The fine-tuning of TRAF2-GSTP1-1 interaction: effect of ligand binding and in situ detection of the complex. De Luca A. et al. **Cell Death Dis. 2014;5:e1015.**
7. New insights into the mechanism of JNK1 inhibition by glutathione transferase P1-1. De Luca A. et al. **Biochemistry. 2012;51(37):7304-12.**
8. The glutathione transferase inhibitor 6-(7-nitro-2,1,3-benzoxadiazol-4-ylthio)hexanol (NBDHEX) increases temozolomide efficacy against malignant melanoma. Tentori L. et al. **Eur J Cancer. 2011;47(8):1219-30.**
9. Structural basis for the binding of the anticancer compound 6-(7-nitro-2,1,3-benzoxadiazol-4-ylthio)hexanol to human glutathione s-transferases. Federici L. et al. **Cancer Res. 2009;69(20):8025-34.**
10. Overcoming resistance to conventional drugs in Ewing sarcoma and identification of molecular predictors of outcome.Scotlandi K. et al. **J Clin Oncol. 2009;27(13):2209-16.**
11. 6-(7-Nitro-2,1,3-benzoxadiazol-4-ylthio)hexanol, a specific glutathione S-transferase inhibitor, overcomes the multidrug resistance (MDR)-associated protein 1-mediated MDR in small cell lung cancer. Filomeni G. et al. **Mol Cancer Ther. 2008;7(2):371-9.**
12. Overcoming glutathione S-transferase P1-related cisplatin resistance in osteosarcoma. Pasello M. et al. **Cancer Res. 2008;68(16):6661-8**.
13. A strong glutathione S-transferase inhibitor overcomes the P-glycoprotein-mediated resistance in tumor cells. Turella P. et al. **J Biol Chem. 2006;281(33):23725-32.**
14. 7-Nitro-2,1,3-benzoxadiazole derivatives, a new class of suicide inhibitors for glutathione S-transferases. Mechanism of action of potential anticancer drugs. Ricci G. et al. **J Biol Chem. 2005;280(28):26397-405**.
15. Proapoptotic activity of new glutathione S-transferase inhibitors. Turella P. et al. **Cancer Res. 2005;65(9):3751-61.**

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ACADEMIC AND SCIENTIFIC CURRICULUM OF PROF. ANNA MARIA CACCURI

PERSONAL DATA
Name and Surname: ANNA MARIA CACCURI
Place and date of birth: Rome, 28th October 1955

***CURRENT POSITION*:** Associate Professor of Biochemistry
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Address: University of Rome "Tor Vergata" via Montpellier 1, -00133 ROMA
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Consulting hours: to be defined
Italian Ministry of Education Academic-Scientific sector: BIO/10 - BIOCHEMISTRY

SCIENTIFIC AND DIDACTIC ACTIVITY

Education and academic positions:
1979 Degree in Biological Science (cum laude) at the University of Rome La Sapienza.
1983 Assistant Professor at the University of Chieti G. D'Annunzio.
1986-2001 Assistant Professor at the University of Rome Tor Vergata.
2001-2018 Associate Professor at University of Rome Tor Vergata.

Professional and didactic activities in Italian and Foreign Institutions:
From 1987 to 1988 she worked as a Post-doc fellow in the

1) Department of Human Biological Chemistry and Genetics of the University of Texas, in the Medical Branch of Galveston (U.S.A.)
2) Department of Biochemistry of the University of Oxford (U.K).

Awards and funding:
2005: research contract: "study of the interaction between the enzyme glutathione S-transferase detoxifying skin and the substances listed in the CE / 39/2000 with the notation 'skin 'aimed at biological monitoring of exposed subjects" funded by ISPESL (Role: PI).
2007-2010 project: "Alliance Against Cancer" funded by the ISS (Role: PI of research unit).
2008 research contract " Identification of Molecular Markers for the development of new diagnostic and therapeutic strategies in the treatment of Mesothelioma" funded by ISPESL (Role: PI).
2010-2013 project: "Exploiting the protein-protein interaction properties of glutathione transferase GSTP1-1 for cancer treatment" funded by AIRC (Role: PI).
2016-2017 project: "Role of the glutathione transferase inhibitor MC3181 in the modulation of the growth and metastatic spreading of cutaneous melanoma" funded by University of Rome "Tor Vergata" Grant: "CONSOLIDATE THE FOUNDATIONS" (Role: PI).
2016-2018 project: "Study of the potential protective role of the enzyme glutathione transferase against retinal neurodegeneration. Analysis of the effect of glycemic variability on retinal glia cells" funded by Italian Ministry of Health (5x1000) and Fondazione Roma (Role PI).

Research activity: 15 selected publications

Since 2002 she has been involved in the design, synthesis and study of potent inhibitors of GSTs characterized by a peculiar mechanism of action and promising anticancer properties.

The new compounds have been included into: United States Patent No. US8,796,317 B2 (USE OF 7-NITRO-2,1,3-BENZOXADIAZOLE DERIVATIVES FOR ANTICANCER THERAPY, Caccuri et al.) and in the Italian Patent No 0001412189 (DERIVATI DEL 7-NITRO-2,1,3-BENZOSSADIAZOLO PER TERAPIA ANTITUMORALE, Mai, Caccuri et al). In particular, among the new derivatives, the compound MC3181 is highly effective against human melanoma cell lines harboring the BRAFV600E mutation and against mutated melanoma cells made resistant to the BRAF inhibitor vemurafenib.

1. The nitrobenzoxadiazole derivative MC3181 blocks melanoma invasion and metastasis. De Luca A. et al. **Oncotarget. 2017;8(9):15520-15538.**
2. New insight into the interaction of TRAF2 C-terminal domain with lipid raft microdomains. Ceccarelli A. et al. **Biochim Biophys Acta. 2017;1862(9):813-822.**
3. A new water soluble MAPK activator exerts antitumor activity in melanoma cells resistant to the BRAF inhibitor vemurafenib. Graziani G. et al **Biochem Pharmacol. 2015;95(1):16-27.**
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6. The fine-tuning of TRAF2-GSTP1-1 interaction: effect of ligand binding and in situ detection of the complex. De Luca A. et al. **Cell Death Dis. 2014;5:e1015.**
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11. 6-(7-Nitro-2,1,3-benzoxadiazol-4-ylthio)hexanol, a specific glutathione S-transferase inhibitor, overcomes the multidrug resistance (MDR)-associated protein 1-mediated MDR in small cell lung cancer. Filomeni G. et al. **Mol Cancer Ther. 2008;7(2):371-9.**
12. Overcoming glutathione S-transferase P1-related cisplatin resistance in osteosarcoma. Pasello M. et al. **Cancer Res. 2008;68(16):6661-8**.
13. A strong glutathione S-transferase inhibitor overcomes the P-glycoprotein-mediated resistance in tumor cells. Turella P. et al. **J Biol Chem. 2006;281(33):23725-32.**
14. 7-Nitro-2,1,3-benzoxadiazole derivatives, a new class of suicide inhibitors for glutathione S-transferases. Mechanism of action of potential anticancer drugs. Ricci G. et al. **J Biol Chem. 2005; 280(28):26397-405**.
15. Proapoptotic activity of new glutathione S-transferase inhibitors. Turella P. et al. **Cancer Res. 2005;65(9):3751-61.**