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Professore Ordinario di Patologia Generale

**DIPARTIMENTO DI SCIENZE BIOMEDICHE
UNITA' DI ONCOLOGIA E PATOLOGIA MOLECOLARE
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ATTIVITA' DIDATTICA A.A. 2019-2020

**Patologia generale e Fisopatologia, CdL Medicina e Chirurgia
Patologia, Immunologia e Patologia Clinica, CdL Scienze Infermieristiche
Eziopatogenesi delle Malattie, CdL Igienisti Dentali
Patologia generale in diverse Scuole di Specializzazione della Facoltà di Medicina**

ESPERIENZE SCIENTIFICHE ALL'ESTERO

1978-81	Post-doctoral Fellow, Department of Pathology, University of Toronto, Canada
1983 (3 mesi)	Visiting Assistant Professor, Dipartimento of Pathology, University of Toronto, Canada
1986 (3 mesi)	Visiting Assistant Professor, Department of Pathology, University of Toronto, Canada
1988 (4 mesi)	Visiting Assistant Professor, Dept. of Pathology, University of Toronto, Canada
June-October 1992	Visiting Professor, Dept. Oncological Pathology, Nara Medical School, Nara, Japan.
June-August 1995	Visiting Professor, Dept. of Pathology, School of Medicine, University of Pittsburgh

ESPERIENZE ACCADEMICHE

1975-77	Vincitore di Borsa di Studio, Regione Autonoma Sardegna, Istituto di Patologia Generale, Facoltà di Medicina, Università di Cagliari, Italy
1978-1980	Borsista CNR, Istituto Di Farmacologia e Patologia Biochimica, Facoltà di Medicina, Università di Cagliari, Italy
1990	Professore Ordinario di Patologia, Facoltà di Medicina
1997-98	Presidente del Corso di Laurea di Odontoiatria e PD (Università di Cagliari)
1999-2006	Presidente del Corso di Laurea di Medicina e Chirurgia, Università di Cagliari
1998-2006	Direttore del programma di Dottorato di Ricerca in Patologia e Tossicologia Ambientale, Università di Cagliari
2001-2016	Coordinatore del Programma Erasmus/Globus della Facoltà di Medicina e Chirurgia, Università di Cagliari.
2007-2009	Direttore del Dottorato di Ricerca in Tossicologia

2009-2012	Direttore del Dipartimento di Tossicologia
2012-2015	Membro del Senato Accademico dell'Università di Cagliari
2015-2019	Coordinatore del Dottorato di Ricerca in Medicina Molecolare e Traslazionale, Università di Cagliari

MEMBRO DELL'EDITORIAL BOARD DELLE SEGUENTI RIVISTE:

- Cancers
- Biomolecules
- Frontiers in Oncology
- Hepatoma
- Gene Expression

MEMBRO DELLE SEGUENTI SOCIETÀ SCIENTIFICHE

- European Association for Cancer Research (EARC)
- American Association for Cancer Research (AACR)
- American Association for the Study of Liver Disease (AASLD)
- Società Italiana di Patologia e Medicina Traslazionale (SIPMeT)
- Società Italiana di Cancerologia (SIC)

ALTRE ATTIVITÀ

- Membro del Comitato Tecnico Scientifico dell'Associazione Italiana Ricerca sul Cancro (AIRC) (2008-2019)
- Reviewer dei progetti AIRC (2008-2019)
- Reviewer di progetti del Ministero dell'Università e della Ricerca Scientifica, Roma, Italy
- Reviewer of progetti del French National Cancer Institute,
- Reviewer of progetti dell'Institut National de la Santé et de la Recherche Medical (INSERM)
- Reviewer di progetti dell'International Union against Cancer
- Reviewer di progetti dell'Wellcome Trust
- Reviewer di progetti del Health and Medical Research Funds of Honk Kong (China),
- Reviewer di progetti della Research Foundation – Flanders (Belgium)

REFEREE DELLE SEGUENTI RIVISTE SCIENTIFICHE

American Journal of Pathology, Cancer Research, Carcinogenesis, Cell Death and Differentiation, Cell Death Disease, Endocrinology, J Clin Invest, Hepatology, Journal of Hepatology, Gastroenterology, Nature Reviews, International Journal of Cancer, Virchows Cell Archives, Experimental Cell Research, The Histochemical Journal, J. Free Radical Research, FEBS Letters ed altre.

COLLOCAZIONE INTERNAZIONALE

Amedeo Columbano é tra i 100.000 "*Most Influential Scientists 2017*" su un campione di 12 milioni di Scienziati

Amedeo Columbano è tra i 26 Scienziati dell'Ateneo inseriti nella classifica del sito www.topitalianscientists.org.

RESPONSABILE SCIENTIFICO/CO-PRINCIPAL INVESTIGATOR DEI SEGUENTI PROGETTI NAZIONALI/INTERNAZIONALE (ULTIMI 20 ANNI)

- **N.I.H. Grant 2003-2008:** "The Transcriptional Basis of Tumor Promotion Co-principal Investigator
- **PRIN 2004-2006:** "Controllo del Ciclo Cellulare da Ligandi di Recettori Nucleari". Coordinatore Nazionale (2004-2006)
- **AIRC IG 2006-2008:** "Ligands of Nuclear Receptors in Liver Cell Proliferation, Survival and Carcinogenesis". Responsabile Scientifico
- **PRIN 2006-2008:** "Controllo del Ciclo Cellulare da Ligandi di Recettori Nucleari". Coordinatore Nazionale.
- **PRIN 2008-2010:** Ruolo dei Ligandi di Recettori Nucleari nel Controllo del Ciclo Cellulare e del Differenziamento". Coordinatore Nazionale
- **N.I.H. Grant 2008-2013:** The Transcriptional basis of tumor promotion. N. 2 RO1 CA104292-06A1. Co-principal Investigator
- **PRIN 2011-2013:** An Integrated Approach to Hepatocellular Carcinoma: From Molecular Pathogenesis to Targeted Therapies. Coordinatore Nazionale
- **AIRC IG 2012-2014:** "Dissecting the multistep process of hepatocarcinogenesis by coupling miR profiling with transcriptome analysis" Responsabile Scientifico
- **AIRC IG 2014-2017:** "NRF2: A driver of human hepatocellular carcinoma?" Responsabile Scientifico
- **Fondazione di Sardegna 2016-2018:** Role of the TR/T3 axis on the development of hepatocellular carcinoma"; Responsabile Scientifico
- **Regione Autonoma Sardegna 2018-2020:** Possibile utilizzo terapeutico dell'ormone tiroideo e dei suoi analoghi nel carcinoma epatocellulare. Responsabile Scientifico (*In corso*)
- **AIRC IG 2018-2022:** "Targeting the T3/thyroid receptor axis: a new therapeutic opportunity for hepatocellular carcinoma; Budget/5 years: 783.000 Euro; Responsabile Scientifico (*In Corso*)

PUBBLICAZIONI SELEZIONATE DEGLI ULTIMI 10 ANNI

1. Andersen JB, Loi R, Perra A, Factor VM, Ledda-Columbano GM, **Columbano A**, Thorgeirsson SS. Progenitor-derived hepatocellular carcinoma model in the rat. *Hepatology*. 2010;51:1401-1409.
2. Kowalik MA, Perra A, Pibiri M, Cocco MT, Samarut J, Plateroti M, Ledda-Columbano GM, **Columbano A**. TRbeta-is the critical thyroid hormone receptor isoform in T3-induced proliferation of hepatocytes and pancreatic acinar cells. *J Hepatol*. October 2010; 53:686-692
3. Kowalik MA, Saliba C, Pibiri M, Perra A, Ledda-Columbano GM, Sarotto I, Ghiso E, Giordano S, **Columbano A**. YAP regulation of adaptive liver enlargement and HCC development. *Hepatology*. 2011, 53:2086-2096
4. Leoni VP, Ledda-Columbano GM, Pibiri M, Saliba C, Perra A, Kowalik MA, Grober OMV, Ravo M, Weisz A, Locker J, Ghiso E, Giordano S, **Columbano A**. Expression of c-jun is not mandatory for mouse hepatocyte proliferation induced by two nuclear receptor ligands: TCPOBOP and T3. *J Hepatol*. 2011;55:1069-1078
5. Tian J, Huang H, Hoffman B, Liebermann DA, Ledda-Columbano GM, **Columbano A**, Locker J. Gadd45 β is an inducible coactivator of transcription that facilitates rapid liver growth in mice. *J Clin Invest*. 2011; 121:4491-502

6. Severino V, Locker J, Ledda-Columbano GM, **Columbano A**, Parente A, Chambery A. Proteomic characterization of early changes induced by triiodothyronine in rat liver. *J Proteome Res.* 2011;10:3212-3224.
7. Petrelli A, Perra A, Schernhuber K, Cargnelutti M, Salvi A, Migliore C, Ghiso E, Benetti A, Barlati S, Ledda-Columbano GM, Portolani N, De Petro G, **Columbano A**, Giordano S. Sequential analysis of multistage hepatocarcinogenesis reveals that miR-100 and PLK1 dysregulation is an early event maintained along tumor progression. *Oncogene.* 2012 ;31:4517-4526
8. Migliore C, Martin V, Leoni VP, Restivo A, Atzori L, Petrelli A, Isella C, Zorcolo L, Sarotto I, Casula G, Comoglio PM, **Columbano A**, Giordano S. MiR-1 Downregulation Cooperates with MACC1 in Promoting MET Overexpression in Human Colon Cancer. *Clin Cancer Res.* 2012, 18:737-747.
9. Giordano S, **Columbano A**. MicroRNAs: New tools for diagnosis, prognosis and therapy in HCC? *Hepatology.* 2013, 57:840-847
10. Fanti M, Singh S, Ledda-Columbano GM, **Columbano A**, Monga SP. Triiodothyronine Induces hepatocyte proliferation by protein kinase A-dependent-b-catenin activation in rodents. *Hepatology.* 2014;59:2309-2320.
11. Giordano S, **Columbano A**. Met as a therapeutic target in HCC: Facts and hopes. *J Hepatol.* 2014;60:442-452.
12. Petrelli A, Perra A, Cora D, Sulas P, Menegon S, Manca C, Migliore C, Kowalik MA, Ledda-Columbano GM, Giordano S, **Columbano A**. MicroRNA/gene profiling unveils early molecular changes and nuclear factor erythroid related factor 2 (NRF2) activation in a rat model recapitulating human hepatocellular carcinoma (HCC). *Hepatology.* 2014;59:228-241
13. Rizzo F, Hashim A, Marchese G, Ravo M, Tarallo R, Nassa G, Giurato G, Rinaldi A, Cordella A, Persico M, Sulas P, Perra A, Ledda-Columbano GM, **Columbano A**, Weisz A. Timed regulation of PIWI-interacting RNAs expression during rat liver regeneration. *Hepatology.* 2014; 60:798-806.
14. Perra A, Kowalik MA, Ghiso E, Ledda-Columbano GM, Di Tommaso L, Angioni MM, Raschioni C, Testore E, Roncalli M, Giordano S, **Columbano A**. YAP activation is an early event and a potential therapeutic target in liver cancer development. *J Hepatol* 2014;61:1088-1096.
15. Frau C, Loi R, Petrelli A, Perra A, Menegon S, Kowalik MA, Pinna S, Leoni VP, Fornari F, Gramantieri L, Ledda-Columbano GM, Giordano S, **Columbano A**. Local hypothyroidism favours the progression of rat preneoplastic lesions to HCC. *Hepatology* 2015;61:249-59.
16. Zavattari P, Perra A, Menegon S, Kowalik MA, Petrelli A, Angioni MM, Follenzi A, Quagliata L, Ledda-Columbano GM, Terracciano L, Giordano S, **Columbano A**. Nrf2, but not β -catenin, mutation represents an early event in rat hepatocarcinogenesis. *Hepatology.* 2015;62:851-62
17. Kowalik MA, Sulas P, Ledda-Columbano GM, Giordano S, **Columbano A**, Perra A. Cytokeratin-19 positivity is acquired along cancer progression and does not predict cell origin in rat hepatocarcinogenesis. *Oncotarget.* 2015;6:38749-63
18. Mattu S, Fornari F, Quagliata L, Perra A, Angioni MM, Petrelli A, Menegon S, Morandi A, Chiarugi P, Ledda-Columbano GM, Gramantieri L, Terracciano L, Giordano S, **Columbano A**. The metabolic gene HAO2 is down regulated in mouse, rat and human hepatocellular carcinoma and correlates with metastasis and poor survival. *J Hepatol* 2016;64:891-8.

19. Kowalik M, Perra A, Ledda-Columbano GM, Piacentini M, **Columbano A**, Falasca L. Induction of autophagy promotes the growth of early preneoplastic rat liver nodules . **Oncotarget** 2016;7:5788-99.
20. Tschuor C, Kachaylo E, Limani P, Raptis DA, Linecker M, Tian Y, Herrmann U, Grabliauskaite K, Weber A, **Columbano A**, Graf R, Humar B, Clavien PA. Constitutive androstane receptor (Car)-driven regeneration protects liver from failure following tissue loss. **J Hepatol.** 2016;65:66-74.
21. Kowalik MA, Guzzo G, Morandi A, Perra A, Menegon S, Masgras I, Trevisan E, Angioni MM, Fornari F, Quagliata L, Ledda-Columbano GM, Gramantieri L, Terracciano L, Giordano S, Chiarugi P, Rasola A, **Columbano A**. Metabolic reprogramming identifies the most aggressive lesions at early phases of hepatic carcinogenesis. **Oncotarget** 2016 May 31;7(22):32375-93.
22. Menegon S, **Columbano A**, Giordano S. NRF2, a Janus molecule in cancer. **Trends Mol Med** 2016;7:578-93.
23. Perra A, Plateroti M, **Columbano A**. T3/TRs axis in hepatocellular carcinoma: new concepts for an old pair. **Endocrine-Related Cancer** 2016;23: R353-69.
24. Angioni MM, Bellofatto K, Merlin S, Menegon S, Perra A, Petrelli A, Sulas P, Giordano S, **Columbano A**, Follenzi A. A long term, non tumorigenic rat hepatocyte cell line and its malignant counterpart, as tools to study hepatocarcinogenesis. **Oncotarget**, 2017; 8:15716-15731
25. Kowalik MA, **Columbano A**, Perra A. Emerging Role of the Pentose Phosphate. Pathway in Hepatocellular Carcinoma. **Front Oncol.** 2017;7:87.
26. Puliga E, Min Q, Tao J, Zhang R, Pradhan-Sundt T, Poddar M, Singh S, **Columbano A**, Yu J, Monga SP. Thyroid Hormone Receptor- β Agonist GC-1 Inhibits Met- β -Catenin-Driven Hepatocellular Cancer. **Am J Pathol.** 2017;187:2473-2485.
27. **Columbano A**, Chiellini G, Kowalik MA. GC-1: A Thyromimetic With Multiple Therapeutic Applications in Liver Disease. **Gene Expr.** 2017;17:265-275.
28. Rossetti A, Togliatto G, Rolo AP, Teodoro JS, Granata R, Ghigo E, **Columbano A**, Palmeira CM, Brizzi MF. Unacylated ghrelin prevents mitochondrial dysfunction in a model of ischemia/reperfusion liver injury. **Cell Death Discov.** 2017 Dec 4;3:17077.
29. Sulas P, Di Tommaso L, Novello C, Rizzo F, Rinaldi A, Weisz A, **Columbano A**, Roncalli M. A Large Set of miRNAs Is Dysregulated from the Earliest Steps of Human Hepatocellular Carcinoma Development. **Am J Pathol.** 2018 Mar;188(3):785-794.
30. Mattu S, Saliba C, Sulas P, Zavattari P, Perra A, Kowalik MA, Monga SP, **Columbano A**. High Frequency of β -Catenin Mutations in Mouse Hepatocellular Carcinomas Induced by a Nongenotoxic Constitutive Androstane Receptor Agonist. **Am J Pathol.** 2018;188:2497-2507.
31. Kowalik MA, **Columbano A**, Perra A. Thyroid Hormones, Thyromimetics and Their Metabolites in the Treatment of Liver Disease. **Front Endocrinol (Lausanne).** 2018;10:9:382.
32. Migliore C, Morando E, Ghiso E, Anastasi S, Leoni VP, Apicella M, Cora' D, Sapino A, Pietrantonio F, De Braud F, **Columbano A**, Segatto O, Giordano S. miR-205 mediates adaptive resistance to MET inhibition via ERFF11 targeting and raised EGFR signaling. **EMBO Mol Med.** 2018;10. pii: e8746.
33. Orrù C, Szydłowska M, Taguchi K, Zavattari P, Perra A, Yamamoto M, **Columbano A**. Genetic inactivation of Nrf2 prevents clonal expansion of initiated cells in a nutritional model of rat hepatocarcinogenesis. **J Hepatol.** 2018;69:635-643.
34. Colorectal cancer early methylation alterations affect the crosstalk between cell and surrounding environment, tracing a biomarker signature specific for this tumor. Fadda A, Gentilini D, Moi L, Barault L, Leoni VP, Sulas P, Zorcolo L, Restivo A, Cabras F,

Fortunato F, Zavattari C, Varesco L, Gismondi V, De Miglio MR, Scanu AM, Colombi F, Lombardi P, Sarotto I, Loi E, Leone F, Giordano S, Di Nicolantonio F, **Columbano A**, Zavattari P. *Int J Cancer*. 2018;143:907-920.

35. Runfola M; Sestito S; Bellusci L; La Pietra V; Maria D'amore V; Kowalik MA; Chiellini G; Gul S; Perra A; **Columbano A**; Marinelli L; Novellino E; Rapposelli S. Design, synthesis and biological evaluation of novel TRbeta selective agonists sustained by ADME-Toxicity analysis. *Eur. J Med. Chem.* 2020 15;188:112006.
36. Kowalik MA, Puliga E, Cabras L, Sulas P, Petrelli A, Perra A, Ledda-Columbano GM, Morandi A, Merlin S, Orrù C, Sanchez-Martin C, Fornari F, Gramantieri L, Parri M, Rasola A, Bellomo E, Sebastian C, Follenzi A, Giordano S, **Columbano A**. Thyroid hormone inhibits hepatocellular carcinoma progression via induction of differentiation and metabolic reprogramming". *J Hepatol* 2020;72:1159-1169.