Curriculum Vitae Dr. Pia Giovannelli

Personal details:
Date of birth: 4 April 1979; **Nationality**: Italian
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Education and training:

- **October 2017:** Specialization in Clinical Pathology and Clinical Biochemistry
- **December 2010:** Qualified as PhD in "Pathology of Signal Transduction" XXIII cycle. Department of Biochemistry, Biophysics and General Pathology, Faculty of Medicine and Surgery - II University of Naples, Italy.
  Thesis titled: "*Role of Androgen Receptor/Filamin A association in androgen-dependent migration of mouse fibroblasts NIH3T3*"
  Advisor: Prof. A. Migliaccio.
- **January 2008**: Qualified as Professional Biologist - University Naples 'Federico II', Italy.
- **July 2007**: Graduated in Biological Science *Summa cum Laude* from the University of Naples 'Federico II', Italy. Advisors: Prof. A. Migliaccio and Prof. R. Frunzio .

Professional experience:

- **May 2018:** Researcher at Department of Precision Medicine, University of Campania "L.Vanvitelli", Naples
- **October 2015-September 2016:** Post Doc position with a fellow funded by Regione Campania POR/FSE 2015. Research project title: "*Identification of new therapeutical target for human brain tumor*". Department of Biochemistry, Biophysics and General Pathology, Faculty of Medicine and Surgery - II University of Naples, Italy. Tutor: Prof. Ciro Abbondanza.
- **January 2014-December 2014:** Post Doc Fellowship funded by PRIN 2010/2011. Research project title: "*Androgens and androgen receptor in fibroblasts and their function in prostate cancer progression*". Department of Biochemistry, Biophysics and General Pathology, Faculty of Medicine and Surgery - II University of Naples, Italy. PI: Professor Gabriella Castoria.
- **January 2013-December 2013:** AIRC fellowship "***Volontari Comitato Basilicata***" Title: "The role of androgen receptor in prostate cancer progression". Department of General Pathology, Second University of Naples, Naples, Italy. Advisor: Prof. Antimo Migliaccio, MD.
- **January 2011-December 2012:** AIRC fellowship "***Coclerici***". Title: "The role of steroid signalling activation in human prostate cancer progression". Department of General Pathology, Second University of Naples, Naples, Italy. Advisor: Prof. Antimo Migliaccio, MD.
- **2007-2010**: PhD programme at the II University of Naples - Department of General Pathology.
- **2006-2007**: Training at the Department of General Pathology - II University of Naples. Experimental Thesis in General Pathology: "*Study of small peptides for the growth and proliferation control in human breast cancer cells*" Supervisors: Prof. F. Auricchio and Prof. A. Migliaccio.

Key words describing past & current research areas: Steroids; growth factors, receptors; signal transduction; cell cycle; invasiveness; breast and prostate cancer; cell differentiation, cell biology, migration, cell proliferation.
Techniques: Protein analysis, cellular and molecular biology: Ligand binding displacement studies for receptor analysis, protein purification, SDS-PAGE, Western blot and immunoprecipitation, in vitro

enzymatic assays, protein-protein interactions. Cell culture and co-culture of primary and immortalized cells, analysis of cell adhesion and invasiveness, gene transcription and viability assays, proliferation and cell cycle analysis, fluorescence and contrast phase microscopy. Nucleic acid manipulation and DNA cloning, PCR sequencing, ChIp assay, transfection. **Animal work:** animal handling and surgery. **Laboratory management**: organisation of protocols and laboratory records, competent in Microsoft and Mac operating systems and applications, database searching. **Language skills**: good command of English (speaking, reading and writing).

Publications:

- **The Androgen Receptor in Breast Cancer. Giovannelli P**, Di Donato M, Galasso G, Di Zazzo E, Bilancio A,Migliaccio A. Front. Endocrinol., 28 August 2018 | https://doi.org/10.3389/fendo.2018.00492
- **High-Throughput Screening Identifies Kinase Inhibitors That Increase Dual Adeno-Associated Viral Vector Transduction In Vitro and in Mouse Retina.** Maddalena A, Dell'Aquila F, **Giovannelli P**, Tiberi P, Wanderlingh LG,Montefusco S, Tornabene P, Iodice C, Visconte F, Carissimo A, Medina DL, Castoria G, Auricchio A. Hum Gene Ther. 2018 Aug;29(8):886-901. doi: 10.1089/hum.2017.220.
- **Estrogens and Their Receptors in Prostate Cancer: Therapeutic Implications.** Di Zazzo E, Galasso G, **Giovannelli P**, Di Donato M, Castoria G. Front Oncol. 2018 Jan 18;8:2. doi: 10.3389/fonc.2018.00002. eCollection 2018.
- **Recent advances on bisphenol-A and endocrine disruptor effects on human prostate cancer.** Di Donato M, Cernera G, **Giovannelli P**, Galasso G, Bilancio A,Migliaccio A, Castoria G. Mol Cell Endocrinol. 2017 Dec 5;457:35-42. doi: 10.1016/j.mce.2017.02.045. Epub 2017 Feb 28.
- **Recent advances on bisphenol-A and endocrine disruptor effects on human prostate cancer.** Di Donato M., Cernera G., **Giovannelli P.**, Galasso G., Bilancio A., Migliaccio A., Castoria G. Mol Cell Endocrinol. 2017 Feb 28. pii: S0303-7207(17)30158-2. doi: 10.1016/j.mce.2017.02.045.
- **Prostate cancer stem cells: the role of androgen and estrogen receptors.** Di Zazzo E., Galasso G., **Giovannelli P.**, Di Donato M., Di Santi A., Cernera G., Rossi V., Abbondanza C., Moncharmont B., Sinisi AA., Castoria G., Migliaccio A. Oncotarget. 2016 Jan 5;7(1):193-208. doi: 10.18632/oncotarget.6220.
- **The dual role of androgen receptor in mesenchymal cells**. **Giovannelli P.**, Di Donato M., Cernera G., Di Santi A., Galasso G., Di Zazzo E., Vitale F., Castoria G., Migliaccio A. Receptors & Clinical Investigation 2015
- **Non-genomic androgen action regulates proliferative/migratory signaling in stromal cells.** Di Donato M., **Giovannelli P.**, Cernera G., Di Santi A., Marino I., Bilancio A., Galasso G., Auricchio F., Migliaccio A., Castoria G. Front Endocrinol (Lausanne). 2015 Jan 19;5:225.
- **Role of non-genomic androgen signalling in suppressing proliferation of fibroblasts and fibrosarcoma cells.** Castoria G., **Giovannelli P.**, Di Donato M., CiociolaA., Hayashi R., Bernal F., Appella E., Auricchio F., and Migliaccio A. Cell Death and Disease (2014) 5, e1548
- **Analysis of the androgen receptor/filamin a complex in stromal cells**. **Giovannelli P**., Di Donato M, Auricchio F, Castoria G. Methods Mol Biol. 2014;1204:109-21 **Book: Steroid Receptors. Methods and Protocol. Holder Springer Methods and Protocols**. Editors: G. Castoria & F. Auricchio.
- **Targeting androgen receptor/Src complex impairs the aggressive phenotype of human fibrosarcoma cells.** Castoria G, **Giovannelli P**, Di Donato M, Hayashi R, Arra C, Appella E, Auricchio F, Migliaccio A. PLoS One. 2013
- **Tyrosine phosphorylation of estradiol receptor by Src regulates its hormone-dependent nuclear export and cell cycle progression in breast cancer cells.**. Castoria G, **Giovannelli P**, Lombardi M, De Rosa C, Giraldi T, de Falco A, Barone MV, Abbondanza C, Migliaccio A, Auricchio F.. *Oncogene* 2012 Nov 15: 31 (46): 4868-77.

- **Polyproline and Tat transduction peptides in the study of the rapid actions of steroid receptors.** Migliaccio A, Castoria G, de Falco A, Bilancio A, **Giovannelli P**, Di Donato M, Marino I, Yamaguchi H, Appella E, Auricchio F. Review Steroids, 2012
- **Targeting rapid action of sex-steroid receptors in breast and prostate cancers. Giovannelli P**, Di Donato M, Giraldi T, Migliaccio A, Castoria G, Auricchio F. Front Biosci (Elite Ed). 2012 Jan 1;4:453-61. Review
- **Targeting rapid action of sex steroid receptors in breast and prostate cancers. Giovannelli P**, Di Donato M, Giraldi T, Migliaccio A, Castoria G, Auricchio F. Front Biosci. 2011 Jun 1;16:2224-32. Review.
- **Androgen-induced cell migration: role of androgen receptor/filamin A association.** Castoria G, D'Amato L, Ciociola A, **Giovannelli P**, Giraldi T, Sepe L, Paolella G, Barone MV, Migliaccio A, Auricchio F. *PLoS One* 2011.6:e17218.
- **Steroid signaling activation and intracellular localization of sex steroid receptors.** Giraldi T, **Giovannelli P**, Di Donato M, Castoria G, Migliaccio A, Auricchio F. J Cell Commun Signal. 2010 Dec;4(4):161-72.
- **Cross talk between epidermal growth factor (EGF) receptor and extra nuclear steroid receptors in cell lines.** Migliaccio A, Castoria G, **Giovannelli P**, Auricchio F. *Mol Cell Endocrinol.* 2010;327:19-24.
- **Cell proliferation regulated by estradiol receptor: Therapeutic implications.** Castoria G, Migliaccio A, **Giovannelli P**, Auricchio F. *Steroids* 2010; 75:524-7.
- **Inhibition of estradiol receptor/Src association and cell growth by an estradiol receptor alpha tyrosine-phosphorylated peptide.** Varricchio L, Migliaccio A, Castoria G, Yamaguchi H, de Falco A, Di Domenico M, **Giovannelli P**, Farrar W, Appella E, Auricchio F*Mol Cancer Res.* 2007;5:1213-21.

Book Chapters:

- **Non genomic action of sex steroids: more questions than answers. Advances in Rapid Sex-Steroid Action New Challenges and New Chances in Breast and Prostate Cancers**; 978-1-4614-1763-7; Springer; Vol. 1; Pagg. 1-15 Castoria G, Migliaccio A, Bilancio A, **Giovannelli P**, Di Donato M, Auricchio F.

Congresses:

- **Effect of New Androgen Receptor Antagonists (SARMs) for the Treatment of Human Prostate Cancer.** Di Donato M., **Giovannelli P.**, Bilancio A., de Falco A., Varchi G., Tesei A., Castoria G.- 2nd Joint Meeting of Pathology and Laboratory Diagnostics, 2014 September 17-20, Palermo, Italy. Am J Pathol 2014, 184(Suppl):S1 AMT18.
- **The Role of the Androgen Receptor in Stromal Cells.** Castoria G., Di Donato M., **Giovannelli P.**, Auricchio F., Migliaccio A. 2nd Joint Meeting of Pathology and Laboratory Diagnostics, 2014 September 17-20, Palermo, Italy. Am J Pathol 2014, 184(Suppl):S1 EMD5
- **Androgen receptor acts as a suppressor of proliferation in stromal cells. P. Giovannelli**, G. Castoria, M.De Donato, A. Migliaccio and F. Auricchio. From General pathology to Molecular and translational medicine – ASIP and SIPMET young scientists meeting. Rome, October 23rd-24th, 2013.
- **Effetti genomici e non genomici dei recettori steroidei nei tumori ormono-dipendenti.** G. Castoria**, P. Giovannelli**, M. Di Donato, A. Migliaccio and F. Auricchio. 36° Congresso Nazionale della Società Italiana di Endocrinologia; Padova (Italy), 5-8 June 2013.
- **New molecules in the study of the rapid actions of steroid receptors.** G. Castoria, **P. Giovannelli**, M. Di Donato, A. Migliaccio and F. Auricchio. 3rd EMBO Conference on 'Cellular Signaling & Molecular Medicine'; Cavtat- Dubrovnik (Croatia), 25-29 May 2012.
- **The role of androgen receptor/Filamin A association in androgen induced cell migration. P. Giovannelli**, T. Giraldi, G. Castoria, A. Migliaccio, F. Auricchio. SIP 2010. XXX

NATIONAL CONGRESS ITALIAN SOCIETY OF PATHOLOGY. Salerno. 14-17 Ottobre 2010. Poster session.

- **Rapid androgen action in epithelial and stromal cells.** G. Castoria, A. Migliaccio, **P. Giovannelli**, T. Giraldi and F. Auricchio. Relazione tenuta al 12th European Congress of Endocrinology (ECE 2010)-Praga, 24-28 April 2010.
- **Novel aspects of signalling activation by steroid hormones in target cells.** G. Castoria, A. Migliaccio, **P. Giovannelli**, T. Giraldi and F. Auricchio. Relazione tenuta al 14th International Congress of Endocrinology (ICE 2010)-Kyoto (Giappone), 26-30 March 2010.
- **Androgen regulation of motility in fibroblasts. Pia Giovannelli**, Tiziana Giraldi, Gabriella Castoria, Antimo Migliaccio and Ferdinando Auricchio. Inflammatory cell signaling mechanisms as therapeutic targets. Inflammation 2010. Lussemburgo, 26-29 gennaio 2010; Poster session.
- **Novel steroid antagonists inhibit the growth of prostate and mammary cancer cell xenografts.** Ricciardi C., **Giovannelli P.,** Giraldi T., Oliviero M. A., A. Migliaccio, G. Castoria and F. Auricchio. 63° Convegno dell'Associazione Italiana di Anatomia ed Istologia- Torino (Italy) 10-12 settembre 2009; Poster session.
- **Hormone-dependent nuclear export of estradiol receptor and DNA synthesis in breast cancer cells.** Giraldi T., **Giovannelli P**., Ricciardi C., Oliviero M. A., Lombardi M., G. Castoria, A. Migliaccio and F. Auricchio. 'Unconventional therapeutic targets in cancer'- 21st Pezcoller Symposium-Trento (Italy), 11-13 giugno 2009- Poster session.

Personal Statement

Dr. Pia Giovannelli has been attending prof. Ferdinando Auricchio's laboratory since April 2006 at the Department of General Pathology, Faculty of Medicine of the Second University of Naples. The interest of the group has been focusing for a long time on the study of the molecular mechanisms by which steroid hormones regulate proliferation and survival of target cells activating circuits of signal transduction, such as Src / Ras / ERKs and PI3-kinase /Akt. The research group of prof. Auricchio has shown that activation of these signals from steroids have effects on the nuclear events which control the progression of G1 / S of target cells. In addition, the activation of these effectors induces changes in the cytoskeleton and controls motility and invasiveness of reproductive cells and not reproductive. The set of data obtained by the research group, in addition to defining the role, modulation, and the interconnections of the signalling pathways activated by steroids in target cells, provided guidance for targeted therapeutic interventions in the treatment of hormone dependent mammary and prostate cancers. Dr Giovannelli focused her attention on studies showing that in human breast carcinoma (MCF-7) and in prostate cancer (LNCaP) derived cells, steroid hormones regulate cell proliferation by activating the pathway of MAPKs. This activation is made possible through the direct interaction between the androgen receptor (AR) or the estradiol receptor (ER) and the cytoplamatic kinase Src. In these cell lines, stimulation with physiological concentrations of estradiol or synthetic androgen R1881 or with the epidermal growth factor (EGF) induces the formation of a ternary complex AR / ER / Src which activates the signaling of MAPKs and induces the DNA synthesis and cell proliferation. These studies gave rise to identification and synthesis of a small peptide of 6 amino acids that mimics the sequence around the residue of phospho-tyrosine in position 537 of the alpha form of the human receptor of estradiol and is capable of inhibiting cell proliferation. The phosphopeptide blockades the interaction ER / Src and inhibits the Src pathway / ERK pathway, the expression of cyclin D and DNA synthesis induced by estradiol, androgen or EGF. Moreover, differently to the classic steroidal antagonists, the peptide does not interfere with the transcriptional activity ER or AR-dependent. The inhibitory effects of the peptide were observed in vivo using xenografts of human breast MCF-7 cancer cells in immunosuppressed mice. These data (Migliaccio et al. 2007) indicate that inhibition of the association between steroid receptors and Src or other effectors of the signal may represent a new therapeutic approach to interfere with the growth of hormone-dependent mammary tumors. In this study, Dr Giovannelli performed many techniques used in the analysis of signal transduction (immunoprecipitates of cell lysates and

immunoprecipitates by Western blot analysis, assay of protein activation involved in signal transduction) and biological effects consequent to their activation (cell cycle regulation, cell survival and analysis of BrdU incorporation by immunofluorescence). Dr. Giovannelli has also investigated a detailed mechanism of ER nuclear export, explaining its involvement in breast cancer proliferation and how the ER/Src complex also plays a pivotal role. In this work, the use of two peptides, one for trapping ER in nucleus and the other for disrupting the ER/Src association, was shown to block breast cancer growth. The results are published in a paper on Oncogene in 2012, were she is co-first author (Castoria et al., 2012). Dr Giovannelli has also contributed with a principal investigator role, to a work focused on the analysis of the molecular mechanisms by which androgens stimulate the migration of murine fibroblasts NIH3T3 and human fibrosarcoma cells HT1080. In these cell lines, androgens block the cell cycle progression and activate cell migration through a mechanism involving the activation of Rac, a small GTP-binding protein. Stimulation of NIH3T3 cells with very low concentrations of androgen (1pm) induces association between AR, Src and PI3K and stimulates cell proliferation. Surprisingly, stimulation with 10nM of androgen blocks the cell cycle progression, it does not lead to the formation of this ternary complex, it activates the monomeric GTP-ase Rac1and induces cytoskeletal changes and cell migration. In this study, Dr Giovannelli has worked closely analyzing the molecular mechanisms regulating androgen-induced cell migration by wound-healing experiments, 'time-lapse video microscopy', transwell assays, RNA interference and pull-down assay. Thanks to this strong experience in the field of breast and prostate cancer, Dr. Pia Giovannelli has all the technical skills and the knowledge required to lead a precise study and obtaine the desired results. Since 2010 she coordinates, together with Prof. Castoria the research group to which it belongs and this is proven by several publications in which she is co-first author. During the last year she focuses her studies on the role of steroid hormones on an brain tumor for identify new therapeutical targets, thanks to a fellow funded by Regione Campania POR/FSE 2015 (Research project title: "*Identification of new therapeutical target for human brain tumor*").
Starting from 2016 she studies the phenomena of drug resistance in Prostate and Breast cancer, in particular her studies are focalized on the role of androgen receptor in Androgen-resistant Prostate cancers and in Triple negative breast cancers.