PERSONAL INFORMATION Chiara Pighi

Occupational Field Immunology and Immunopathology

EDUCATION, TRAINING AND RESEARCH EXPERIENCE

February 2019 – present

Research Fellow at Sapienza University of Rome, Dept. of Experimental Medicine.

February 2018 – February 2019

Research Fellow at Sapienza University of Rome, Dept. of Experimental Medicine.

Project title: "**Interplay between NK cells and tumor-targeting anti-CD20 mAbs: impact of FcgammaRIIIA/CD16 affinity ligation conditions on epigenetic-based NK reprogramming**". Supervisor: Professor Ricciarda Galandrini.

My research activity has been mainly focused on the analysis of the molecular mechanisms underlying the priming of human Natural Killer (NK) cells for IFN-gamma production upon high affinity CD16 receptor ligation. In particular, I investigated whether post-transcriptional as well as epigenetic or signalling modifications may account for the primed status of NK cells dictated by the high affinity CD16 ligation conditions. Moreover, I am carrying out studies aimed at exploring the impact of monoclonal antibody-based therapeutic regimens or autoimmune pathologic conditions on in vivo dynamics and anti-tumor relevance of memory NK cells.

November 2014 – February 2018

PhD in Immunological, Hematological and Rheumatic Sciences.

Laboratory of Immunology and Immunopathology directed by Professor Angela Santoni, under the supervision of Professor Ricciarda Galandrini. Dept. of Experimental Medicine, Sapienza University of Rome – Viale Regina Elena 324, 00161 Rome (Italy).

Research interest has been mainly focused on the analysis of the effects induced on human Natural Killer (NK) cells by tumor B cells coated with anti-CD20 therapeutic antibodies, widely used in the treatment of B cell-malignancies and autoimmune disorders. In particular, I investigated the dynamics of FcgammaRIIIA/CD16 receptor in primary NK cells during cytolytic interactions with anti-CD20-opsonised targets and the impact of receptor trafficking on NK functions. My studies identified novel molecular mechanisms responsible for CD16-mediated NK cell desensitization induced by anti-CD20 antibodies. Subsequently my research activity has been focused on understanding the cellular and molecular mechanisms underlying the modulation of NK cell responsiveness and plasticity induced by anti-CD20 therapeutic antibodies endowed with different binding affinity for CD16 receptor. My studies demonstrated that: 1. CD16 aggregation conditions mediated by rituximab (low affinity) or glycoengineered obinutuzumab (high affinity) may dictate both the amplitude of NK responsiveness and the ability to shift the NK function program: 2. anti-CD20 antibodies drive the selective *in vitro* expansion of the recently identified memory NK cells, highlighting the impact of donor HCMV serostatus and CD16 affinity ligation conditions on this event.
Research thesis: "**Impact of anti-CD20 tumor-targeting therapeutic monoclonal antibodies on human Natural Killer cell responsiveness and plasticity: relevance of FcgammaRIIIA/CD16 affinity ligation conditions**". Training coordinator: Professor Ricciarda Galandrini

May 2011 – October 2014

Student Internship at Laboratory of Immunology and Immunopathology directed by Professor Angela Santoni, under the supervision of Professor Ricciarda Galandrini.

Dept. of Experimental Medicine, Sapienza University of Rome – Viale Regina Elena 324, 00161 Rome (Italy)

January 2012 – July 2014

Master degree in Medical Biotechnology.

110/110 cum laude

Sapienza University of Rome - Piazzale Aldo Moro 5, 00185 Rome (Italy)

Principal subjects: Bioinformatics; Biotechnology of human reproduction; Cardiology; Cell biotechnology; Embryology; Endocrinology; Hematology; Human genetics; Immunology; Immunopathology; Molecular biology; Molecular diagnostic and imaging; Molecular medicine; Molecular oncology; Parasitology; Pathology; Virology.

Research thesis: "**CD16 aggregation induced by anti-CD20 therapeutic antibodies promotes an hyporesponsive status in human NK cells**". Training coordinator: Professor Ricciarda Galandrini

My Master degree thesis focuses on the study of the functional outcome of CD16 aggregation induced by anti-CD20-opsonised target cells in primary human NK cells. In particular, we addressed whether rituximab or ofatumumab dependent CD16 aggregation may promote the exhaustion of NK cells leading to resistance to anti-CD20 antibodies based therapy.

Techniques used: Cell cultures. Cytofluorimetry. Citotoxicity assay. ELISA assay.
Fluorescence Microscopy. Immunoprecipitation. Protein extraction. Western Blotting.

October 2008 - November 2011

Bachelor degree in Biotechnology.

110/110 cum laude

Sapienza University of Rome - Piazzale Aldo Moro 5, 00185 Rome (Italy)

Principal subjects: Biochemistry; Bioinformatics; Cellular Biology; Chemistry; Development Biology; General Pathology; Genetics; Immunology; Molecular Biology; Physics.

Research thesis: "**Cytofluorimetric analysis of modulation of the activating receptor NKG2D expression in primary human NK cells induced by target cell recognition**". Training coordinator: Professor Ricciarda Galandrini

My Bachelor degree thesis focuses on the set up of the experimental conditions to understand if the activating receptor NKG2D undergoes endocytosis processes followed by recycling upon interaction with ligands MICA and ULBP2 and if these processes are functional to the maintenance of the cytotoxic potential.

Techniques used: Cell cultures. Citotoxicity assay. Flow Cytofluorimetry. Fluorescence Microscopy. Immunoprecipitation. Protein extraction. Western Blotting.

September 2003- July 2008

High school degree.

100/100 cum laude

Liceo Scientifico "Bertrand Russell" - Via Tuscolana 208, 00182 Rome (Italy)

Principal subjects: Mathematics, Physics, Biology, Chemistry, Italian, Latin, English, Philosophy, History, Law and Art.

PERSONAL SKILLS

Mother tongue(s): Italian

Other language(s)

	UNDERSTANDING		SPEAKING		WRITING
	Listening	Reading	Spoken interaction	Spoken production	
English	B2	B2	B1	B1	B2

Levels: A1/2 Basic User - B1/2 Independent User - C1/2 Proficient User
Common European Framework of Reference for Languages

Personal skills: Outgoing, curious, optimistic, always looking for new challenges and learning.
High propensity to work towards goals, and manage projects.
Maximum flexibility and availability of a comparison.

Job-related skills:
Cell cultures
PBMC isolation and depletion of cellular subpopulations.
Flow cytometry
Fluorescence microscopy
Cytotoxicity assay
ELISA assay
Protein extraction
Western blotting
Immunoprecipitation
Genomic DNA or RNA extraction
mRNA analysis (mRNA reverse transcription and qPCR)
miRNA analysis (miRNA reverse transcription and qPCR)

Computer skills:
Microsoft Office™ suite (Word, Excel, PowerPoint)
Adobe™ suite (PhotoShop)
Data Analysis (Axio Vision, BD CellQuest, FlowJo, ImageJ, Prism)
Basic Knowledge: Bioinformatics

Driving licence: B, own car.

ADDITIONAL INFORMATION

Memberships

Italian Society of Immunology, Clinical Immunology and Allergology (SIICA)

Fundings

Sapienza University Funding for Start Research Project (2019-2020). Project title: "**Characterization of tumor recognition capability of memory NK cells and their dependence on immune checkpoints: relevance for direct and therapeutic antibody-mediated anti-tumor activity".** Protocol n°: AR21916B74238026

Sapienza University Funding for Start Research Project (2018-2019). Project title: "**Analysis of the molecular mechanisms underlying the priming of NK cells for IFN-gamma production upon high affinity CD16 ligation: role of miRNAs in a therapeutic setting".** Protocol n°: AR218164182E4EF7

Sapienza University Funding for Start Research Project (2016-2017). Project title: "**The interplay between anti-CD20 therapeutic antibodies and human natural killer cells: impact of antibody Fc engineering".** Protocol n°: AR116154C910E751

Student supervision

2014-present

I supervised ungraduated students of Laboratory Technician and Biotechnology for their experimental training and thesis's drafting. I did lessons at Liceo Scientifico "Pacinotti-Archimede" (Via Montaione 15, 00139, Rome, Italy) as part of the project "Biologia con curvatura biomedica" AA 2018-2019.

Other scientific activities

I was part of the organizing scientific committee of the 8th Biology and Molecular Medicine (BEMM) PhD School Symposium, which was held on 20th November 2017 at Sapienza University of Rome.

Publications

(Impact Factor reference 2019 JCR Science Edition)

Capuano C, Romanelli M, **Pighi C**, Cimino G, Rago A, Molfetta R, Paolini R, Santoni A, Galandrini R. **Anti-CD20 Therapy Acts via FcγRIIIA to Diminish Responsiveness of Human Natural Killer Cells**. *Cancer Res. 2015;75(19):4097-108. doi:10.1158/0008-5472.CAN-15-0781. IF: 9.72*

Capuano C*, **Pighi C***, Molfetta R, Paolini R, Battella S, Palmieri G, Giannini G, Belardinilli F, Santoni A, Galandrini R. **Obinutuzumab-mediated high-affinity ligation of FcγRIIIA/CD16 primes NK cells for IFNγ production.** *Oncoimmunology. 2017;6(3):e1290037. doi:10.1080/2162402X.2017.1290037. IF: 5.86* ***(*) equal contribution***

Capuano C, Battella S, **Pighi C**, Franchitti L, Turriziani O, Morrone S, Santoni A, Galandrini R, Palmieri G**. Tumor-Targeting Anti-CD20 Antibodies Mediate In Vitro Expansion of Memory Natural Killer cells: Impact of CD16 affinity Ligation Conditions and In Vivo Priming.** *Front. Immunol. 2018;9:1031. doi:10.3389/fimmu.2018.01031. IF: 5.08*

(*Review Article*) Capuano C, **Pighi C**, Battella S, Santoni A, Palmieri G, Galandrini R. **Memory NK cell features exploitable in anti-cancer immunotherapy**. *J Immunol Res. 2019; 2019:8795673. doi:10.1155/2019/8795673. IF: 3.32*

Battella S, Oliva S, Franchitti L, La Scaleia R, Soriani A, Isoldi S, Capuano C, **Pighi C**, Morrone S, Galandrini R, Santoni A, Palmieri G. **Fine tuning of the DNAM-1/TIGIT/ligand axis in mucosal T cells and its dysregulation in pediatric inflammatory bowel diseases (IBD).** *Mucosal Immunol. 2019. doi:10.1038/s41385-019-0208-7. IF: 6.72*

Capuano C*, **Pighi C***, Maggio R, Battella S, Morrone S, Palmieri G, Santoni A, Klein C, Galandrini R. **CD16 pre-ligation by defucosylated tumor-targeting mAb sensitizes Natural Killer cells to γc cytokine stimulation via PI3K/mTOR axis**. *Cancer Immunol Immunother. 2020. doi: 10.1007/s00262-020-02482-2. IF: 5.44* ***(*) equal contribution***

Abstracts

(Impact Factor reference 2019 JCR Science Edition)

C. Pighi, C. Capuano, R. Maggio, S. Battella, S. Morrone, G. Palmieri, A. Santoni, C. Klein, R. Galandrini. **CD16 aggregation in high affinity conditions by tumor-targeting mAb obinutuzumab promotes a PI3K/mTORdependent priming of Natural Killer cells for IFN-gamma production, associated to miR-155 upregulation.** II Joint Meeting of the German Society for Immunology (DGfI) and the Italian Society of Immunology, Clinical Immunology and Allergology (SIICA). Eur J Immunol, Vol.49. Suppl. no 1. Page 271-72. doi:10.1002/eji.201970300. Munich, September 10-13, 2019.IF: 4.40

C. Capuano, M. Romanelli, **C. Pighi**, R. Molfetta, R. Paolini, A. Rago, G. Cimino, A. Santoni, R. Galandrini. **A sustained CD16 aggregation induced by therapeutic antibody-opsonised targets impairs cytotoxic responses in human NK cells.** 13th Congress of the Italian Society of Experimental Hematology. Haematologica, Vol.99. Suppl. no 2. Page S47. ISSN 0390-6078. Rimini, October 15-17, 2014. IF: 7.11

Capuano C, Romanelli M, **Pighi C**, Molfetta R, Paolini R, Santoni A and Galandrini R. **CD16 aggregation induced by therapeutic antibody-opsonised targets impairs cytotoxic responses in human NK cells.** Front. Immunol. 15th International Congress of Immunology. Milano, August 22-27, 2013. doi: 10.3389/conf.fimmu.2013.02.00148. IF: 5.08

Abstract for Congress

15th INTERNATIONAL CONGRESS OF IMMUNOLOGY. Milano, Italy August 22-27 2013. "**CD16 aggregation induced by therapeutic antibody-opsonised targets impairs cytotoxic responses in human NK cells**". C. Capuano, M. Romanelli, **C. Pighi**, R. Molfetta, R. Paolini, A. Santoni, R. Galandrini

14th MEETING OF THE SOCIETY FOR NATURAL IMMUNITY. Heidelberg, Germany Sept. 18-22 2013. "**CD16 aggregation induced by therapeutic antibody-opsonised targets impairs cytotoxic responses in human NK cells**". C. Capuano, M. Romanelli, **C. Pighi**, R. Molfetta, R. Paolini, A. Santoni, R. Galandrini

9th NATIONAL CONFERENCE OF THE ITALIAN SOCIETY OF IMMUNOLOGY, CLINICAL IMMUNOLOGY AND ALLERGOLOGY. Firenze, Italy May 28-31 2014. "**A sustained CD16 aggregation induced by therapeutic antibody opsonised targets impairs cytotoxic responses in human NK cells**". C. Capuano, M. Romanelli, **C. Pighi**, R. Molfetta, R. Paolini, A. Santoni, R. Galandrini

13th NATIONAL CONGRESS OF THE ITALIAN SOCIETY OF EXPERIMENTAL HEMATOLOGY. Rimini, Italy Oct. 15-17 2014. "**CD16 aggregation induced by the interaction of human NK cells with therapeutic antibody opsonised target cells leads a persistent reduction of cytotoxic potential**". C. Capuano, M. Romanelli, **C. Pighi**, R. Molfetta, R. Paolini, A. Rago, G. Cimino, A. Santoni, R. Galandrini

10th NATIONAL CONFERENCE OF THE ITALIAN SOCIETY OF IMMUNOLOGY, CLINICAL IMMUNOLOGY AND ALLERGOLOGY. Abano Terme, Italy May 25-28 2016. "**The interplay between anti-CD20 therapeutic antibodies and human natural killer cells: impact of antibody Fc engineering**". **C. Pighi**, C. Capuano, R. Molfetta, R. Paolini, A. Santoni, R. Galandrini

16th MEETING OF THE SOCIETY FOR NATURAL IMMUNITY. Taormina, Italy Oct. 2-5 2016. "**The interplay between anti-CD20 therapeutic antibodies and human natural killer cells: impact of antibody Fc engineering**". C. Capuano, **C. Pighi**, R. Molfetta, R. Paolini, S. Battella, G. Palmieri, G. Giannini, F. Belardinilli, A. Santoni, R. Galandrini

11th NATIONAL CONFERENCE OF THE ITALIAN SOCIETY OF IMMUNOLOGY, CLINICAL IMMUNOLOGY AND ALLERGOLOGY. Bari, Italy May 28-31 2017. "**The interplay between anti-CD20 therapeutic antibodies and "memory" natural killer cells**". C. Capuano, S. Battella, **C. Pighi**, L. Franchitti, A. Santoni, R. Galandrini, G. Palmieri

2nd SPECIAL CONFERENCE EACR AACR SIC (EAS). Firenze, Italy June 24-27 2017. "**The interplay between anti-CD20 therapeutic antibodies and human natural killer cells: impact of antibody Fc engineering**". C. Capuano, **C. Pighi**, R. Molfetta, R. Paolini, S. Battella, G. Palmieri, G. Giannini, F. Belardinilli, A. Santoni, R. Galandrini

5th INTERNATIONAL CONFERENCE OF TRANSLATIONAL MEDICINE ON PATHOGENESIS AND THERAPY OF IMMUNOMEDIATED DISEASES. Milano, Italy May 16-18 2019. "**The glycoengineered tumor-targeting mAb obinutuzumab acts via FcgammaRIIIA/CD16 to promote miR-155 upregulation associated to the priming for IFN-gamma production in Natural Killer cells**". C. Capuano, **C. Pighi**, R. Maggio, S. Battella, S. Morrone, G. Palmieri, A. Santoni, C. Klein, R. Galandrini.

2nd JOINT MEETING OF THE GERMAN SOCIETY FOR IMMUNOLOGY (DGfI) AND THE ITALIAN SOCIETY OF IMMUNOLOGY CLINICAL IMMUNOLOGY AND ALLERGOLOGY (SIICA). Munich, Germany September 10-13 2019. **"CD16 aggregation in high affinity conditions by tumor-targeting mAb obinutuzumab promotes a PI3K/mTOR-dependent priming of Natural Killer cells for IFN-gamma production, associated to miR-155 upregulation". Pighi C**, Capuano C, Maggio R, Battella S, Morrone S, Palmieri G, Santoni A, Klein C, Galandrini R.

Courses and Marks

Master degree in Medical Biotechnology – First Class Honors (110/110 cum laude):
Immunologia e immunopatologia – Patologia molecolare e cellulare (30/30 cum laude)
Biotecnologie cellulari (30/30 cum laude)
Basi molecolari delle funzioni cellulari (30/30 cum laude)
Biochimica e biologia strutturale (30/30 cum laude)
Virologia e parassitologia molecolare (30/30 cum laude)
Scienze e tecniche morfo-funzionali avanzate (30/30 cum laude)
Medicina molecolare e modelli animali di malattia – Medicina rigenerativa (30/30 cum laude)
Patologia genetica e genetica umana – Biotecnologie della riproduzione umana (30/30 cum laude)
Farmacologia e terapie molecolari (30/30 cum laude)
Diagnostica di laboratorio e molecolare – Diagnostica molecolare e imaging (30/30 cum laude)
Applicazione delle tecnologie genomiche in biomedicina (30/30 cum laude)
Principi di bioetica deontologica diritto ed economia aziendale – Strumentazione organizzazione e sicurezza di laboratorio (30/30 cum laude)

Bachelor degree in Biotechnology – First Class Honors (110/110 cum laude):
Chimica generale e inorganica (30/30 cum laude)
Biologia cellulare (30/30 cum laude)
Fisica (30/30)
Matematica e uso dei calcolatori (30/30 cum laude)
Genetica (30/30)
Biotecnologie cellulari e istologia (30/30)
Chimica fisica (30/30 cum laude)
Biologia molecolare (30/30)
Biochimica (30/30 cum laude)
Fisica applicata (30/30)
Fisiologia (30/30 cum laude)
Microbiologia I (28/30)
Chimica analitica (30/30)
Farmacologia (30/30 cum laude)
Immunologia (30/30 cum laude)
Chimica organica (26/30)
Patologia generale (30/30)
Tecnologie ambientali (30/30)
Biologia dello sviluppo (30/30 cum laude)
Ecologia (30/30 cum laude)
Chimica farmaceutica e tecnologie farmaceutiche (28/30)
Microbiologia generale e biotecnologie microbiche (30/30 cum laude)
Virologia (28/30)
Biochimica industriale (30/30)
Aspetti economici e legislativi (30/30)
Bioetica (28/30)
Microbiologia industriale e delle fermentazioni (30/30)

ANNEXES

- Bachelor degree certificate
- Master degree certificate
- PhD certificate

Personal data

I authorize the use of my personal data pursuant to Legislative Decree 30 June 2003, n. 196 "Code regarding the protection of personal data"

In fede
F.to Chiara Pighi

Roma, 31.01.2021