Updated 29/04/22

Curriculum Vitae

Renato Ostuni, PhD

PERSONAL INFORMATION

Name:	Renato Ostuni
Date of birth:	19/04/1983
Nationality:	Italian
ORCID:	0000-0003-0460-3426
Scopus ID:	35094376200
Address:	San Raffaele Telethon Institute for Gene Therapy (SR-Tiget) San Raffaele Scientific Institute Via Olgettina 58, 20132 Milano – Italy
Phone:	+39 02 2643 5017
E-mail:	ostuni.renato@hsr.it
Twitter:	@OstuniLab
Lab website:	https://bit.ly/3thPkBK

CURRENT POSITIONS

2019-present **Assistant Professor** of Tissue Biology
Vita-Salute San Raffaele University, Milan, Italy

2015-present **Group Leader** | Genomics of the Innate Immune System Unit
San Raffaele Telethon Institute for Gene Therapy (SR-Tiget)
San Raffaele Scientific Institute, Milan, Italy

EDUCATION

2008-2010 **Ph.D. in Translational and Molecular Medicine**
University of Milano-Bicocca, Milan, Italy

2005-2007 **M.Sc. in Industrial Biotechnology** (110/110 cum laude)
University of Milano-Bicocca, Milan, Italy

2002-2005 **B.Sc. in Biotechnology** (110/110 cum laude)
University of Milano-Bicocca, Milan, Italy

PAST POSITIONS

2011-2015 **Postdoctoral Fellow** | Laboratory of **Gioacchino Natoli**
European Institute of Oncology (IEO), Milan, Italy

06/2012 **Postdoctoral Fellow (visiting)** | Laboratory of **Ido Amit**
Weizmann Institute of Science, Rehovot, Israel

2008-2010 **PhD Student** | Laboratory of **Francesca Granucci** and **Ivan Zanoni**
University of Milano-Bicocca, Milan, Italy

HONORS AND AWARDS

2019	Alessandro Moretta Young Investigator Award, Aegean Conferences
2018	Young Investigator Award, European Macrophage and Dendritic Cell Society
2017	European Research Council (ERC) Starting Grant (X-TAM, 759532)
2017	LaboSpace Prize, Italian Society of Immunology and Allergology (SIICA)
2013	Bioeconomy Rome Award, CNCCS Consortium
2012	European Molecular Biology Organization (EMBO) Short-Term Fellowship
2011-2015	European Union FP7th Structured International Post Doc (SIPOD) Fellowship
2008-2010	National PhD Fellowship, Italian Ministry of Health and Research

TEACHING ACTIVITIES

2019 - present	Histology | Master's Degree in Medicine and Surgery Vita-Salute San Raffaele University, Milan, Italy
2015 - present	Laboratory course of Histology | Master's Degree in Medicine and Surgery Cell Therapy (lecturer) | M.Sc. in Biotechnology and Medical Biology Vita-Salute San Raffaele University, Milan, Italy
2013 - 2015	Genomics (lecturer) | Ph.D. in Molecular Oncology | IFOM-IEO, Milan, Italy
2010 - 2012	Molecular Immunology (lecturer) | M.Sc. in Biotechnology University of Milano-Bicocca, Milan, Italy

ACADEMIC SUPERVISION

Postdocs	Marco Genua (2016-); Elisa Montaldo (2016-); Nicoletta Caronni (2018-); Giulia Barbiera (bioinformatician, 2017-); Eleonora Lusito (bioinformatician, 2019-)
Phd students	Valentina Bianchessi (2016-2019); Francesco Cilenti (2018-2021); Francesco Vittoria (2020-); Vincenzo Cuzzola (2021-); Federica Laterza (bioinformatician, 2021-); Carlo Leonardi (bioinformatician, 2021-)

PROFESSIONAL ACTIVITIES AND COMMISSIONS OF TRUST

2021-	Panel Member | Microbiology and Immunology Flanders Research Foundation (FWO), Belgium
2018-	Panel Member | Biomedical Research' and Young Researchers' Grants Scientific and Technical Committee of the Italian MoH
2019-	Coordinator | Organizing Committee of the Ospedale San Raffaele Retreat
2014-	Reviewer | Nature Immunology, Science Immunology, Blood, Cell Reports, eLife, Journal of Leukocyte Biology | Italian MoH, Wellcome Trust, Swiss Cancer League, European Research Council (ERC), French National Research Agency (ANR)

FUNDING

2019-2026	5x1000 Program, AIRC - Partner
2018-2023	Starting Grant #759532, European Research Council (ERC) - PI
2018-2023	My First AIRC Grant (MFAG) #20247, AIRC - PI
2018-2021	'Giovani Ricercatori' Grant #2016-02362156, Italian MoH - PI
2017-2020	Infect-ERA Grant #126, ERA-NET - Partner
2016-2019	SR-Tiget Grant Award F04, Telethon Foundation - PI
2016-2019	'Giovani Ricercatori' Grant #2015-0990, Cariplo Foundation - PI

INVITED PRESENTATIONS (2017-2022)

Human Technopole, Milan; Early Career Immunology Seminars, virtual; Keystone Symposia on Single Cell Biology, Florence (IT); French Dendritic Cell Society (CFCD) meeting, Paris (France); Johns Hopkins Immunology Forum, virtual; Italian Network for Cancer Biotherapy (NIBIT) Meeting (chair), virtual; Epigenetics of Immunity in Cancer (EPIC) Symposium, virtual; Future of Immunology, Berlin, (Germany) (postponed); XVI Congress of Italian Federation of Life Sciences (FISV), Naples (Italy) (postponed); 17th International Congress of Immunology (IUIS), Beijing (China); Italian Association of Cell Cultures (AICC) Meeting, Catanzaro (Italy); Aegean Conferences, 16th International Innate Immunity Conference, Rhodes (Greece); Keystone Symposia, Transcription and RNA Regulation in Inflammation and Immunity, (USA); European Institute of Oncology (IEO)-Alumni meeting, Milan (Italy); European Macrophage and Dendritic cell Society (EMDS) Meeting, Verona (Italy); International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste (Italy); National Institute of Molecular Genetics (INGM), Milan (Italy); Singapore Immunology Network (Singapore); National Congress of Italian Society of Immunology and Allergology (SIICA), Bari (Italy).

PUBLICATIONS (in reverse chronological order)

33 articles | total citations: 4,972 | 4 articles > 500 times; 10 articles > 100 times | H-index: 26
* denotes equal contribution; § denotes corresponding authorship

PRIMARY RESEARCH ARTICLES

1. **DNA damage contributes to neurotoxic inflammation in Aicardi-Goutières syndrome astrocytes.** Giordano AMS, Luciani M, Gatto F, Abou Alezz M, Beghè C, Della Volpe L, Migliara A, Valsoni S, Genua M, Dzieciatkowska M, Frati G, Tahraoui-Bories J, Giliani SC, Orcesi S, Fazzi E, Ostuni R, D'Alessandro A, Di Micco R, Merelli I, Lombardo A, Reijns MAM, Gromak N, Gritti A, Kajaste-Rudnitski A.
   J Exp Med. 2022 | 10.1084/jem.20211121
2. **CRISPR-based gene disruption and integration of high-avidity, WT1-specific T cell receptors improve antitumor T cell function.** Ruggiero E, Carnevale E, Prodeus A, Magnani ZI, Camisa B, Merelli I, Politano C, Stasi L, Potenza A, Cianciotti BC, Manfredi F, Di Bono M, Vago L, Tassara M, Mastaglio S, Ponzoni M, Sanvito F, Liu D, Balwani I, Galli R, Genua M, Ostuni R, Doglio M, O'Connell D, Dutta I, Yazinski SA, McKee M, Arredouani MS, Schultes B, Ciceri F, Bonini C.
   Sci Transl Med. 2022 | 10.1126/scitranslmed.abg8027
3. **A PGE_2-MEF2A axis enables context-dependent control of inflammatory gene expression.** Cilenti F, Barbiera G, Caronni N, Iodice D, Montaldo E, Barresi S, Lusito E, Cuzzola V, Vittoria FM, Mezzanzanica L, Miotto P, Di Lucia P, Lazarevic D, Cirillo DM, Iannacone M, Genua M, Ostuni R§.
   Immunity. 2021 | 10.1016/j.immuni.2021.05.016
4. **Induction of OCT2 contributes to regulate the gene expression program in human neutrophils activated via TLR8.** Tamassia N, Bianchetto-Aguilera F, Gasperini S, Polletti S, Gardiman E, Ostuni R, Natoli G, Cassatella MA.
   Cell Rep. 2021 | 10.1016/j.celrep.2021.109143
5. **TIM4 expression by dendritic cells mediates uptake of tumor-associated antigens and anti-tumor responses.** Caronni N, Piperno GM, Simoncello F, Romano O, Vodret S, Yanagihashi Y, Dress R, Dutertre CA, Bugatti M, Bourdeley P, Del Prete A, Schioppa T, Mazza EMC, Collavin L, Zacchigna S, Ostuni R, Guermonprez P, Vermi W, Ginhoux F, Bicciato S, Nagata S, Benvenuti F.
   Nat Commun. 2021 | 10.1038/s41467-021-22535-z
6. **Co-option of Neutrophil Fates by Tissue Environments.** Ballesteros I, Rubio-Ponce A, Genua M, Lusito E, Kwok I, Fernández-Calvo G, Khoyratty TE, van Grinsven E, González-Hernández S, Nicolás-Ávila JÁ, Vicanolo T, Maccataio A, Benguría A, Li JL, Adrover JM, Aroca-Crevillen A, Quintana JA, Martín-Salamanca S, Mayo F, Ascher S, Barbiera G, Soehnlein O, Gunzer M, Ginhoux F, Sánchez-Cabo F, Nistal-Villán E, Schulz C, Dopazo A, Reinhardt C, Udalova IA, Ng LG, Ostuni R, Hidalgo A.
   Cell. 2020 | 10.1016/j.cell.2020.10.003
7. **Tumor-derived prostaglandin E2 promotes p50 NF-kB-dependent differentiation of monocytic MDSCs.** Porta C, Consonni FM, Morlacchi S, Sangaletti S, Bleve A, Totaro MG, Larghi P, Rimoldi M, Tripodo C, Strauss L, Banfi S, Storto M, Pressiani T, Rimassa L, Tartari S, Ippolito A, Doni A, Soldà G, Duga S, Piccolo V, Ostuni R, Natoli G, Bronte V, Balzac F, Turco E, Hirsch E, Colombo MP, Sica A.
   Cancer Res. 2020 | 10.1158/0008-5472.CAN-19-2843
8. **Dynamics and genomic landscape of $CD8^+$ T cells undergoing intrahepatic priming.** Bénéchet AP, De Simone G, Di Lucia P, Cilenti F, Barbiera G, Le Bert N, Fumagalli V, Lusito E, Moalli F, Bianchessi V, Andreata F, Zordan P, Bono E, Giustini L, Bonilla WV, Bleriot C, Kunasegaran K, Gonzalez-Aseguinolaza G, Pinschewer DD, Kennedy PTF, Naldini L, Kuka M, Ginhoux F, Cantore A, Bertoletti A, Ostuni R*, Guidotti LG*, Iannacone M*.
   Nature. 2019 | 10.1038/s41586-019-1620-6
9. **Immune signature drives leukemia escape and relapse after hematopoietic cell transplantation.** Toffalori C, Zito L, Gambacorta V, Riba M, Oliveira G, Bucci G, Barcella M, Spinelli O, Greco R, Crucitti L, Cieri N, Noviello M, Manfredi F, Montaldo E, Ostuni R, Naldini M, Gentner B, Waterhouse M, Zeiser R, Finke J, Hanoun M, Beelen D, Gojo I, Luznik L, Onozawa M, Teshima T, Devillier R, Blaise D, Halkes C, Griffioen M, Carrabba M, Bernardi M, Peccatori J, Barlassina C, Stupka E, Lazarevic D, Tonon G, Rambaldi F, Cittaro D, Bonini C, Fleischhauer K, Ciceri F, Vago L.
   Nat Med. 2019 | 10.1038/s41591-019-0400-z
10. **Interferon gene therapy reprograms the leukemia microenvironment inducing protective immunity to multiple tumor antigens.** Escobar G, Barbarossa L, Barbiera G, Norelli M, Genua M, Ranghetti A,

Plati T, Camisa B, Brombin C, Cittaro D, Annoni A, Bondanza A, Ostuni R, Gentner B, Naldini L.
Nat Commun. 2018 | 10.1038/s41467-018-05315-0

11. **Monocyte-derived IL-1 and IL-6 are differentially required for cytokine-release syndrome and neurotoxicity due to CAR T cells.** Norelli M, Camisa B, Barbiera G, Falcone L, Purevdorj A, Genua M, Sanvito F, Ponzoni M, Doglioni C, Cristofori P, Traversari C, Bordignon C, Ciceri F, Ostuni R, Bonini C, Casucci M, Bondanza A.
Nat Med. 2018 | 10.1038/s41591-018-0036-4
12. **Opposing macrophage polarization programs show extensive epigenomic and transcriptional cross-talk.** Piccolo V, Curina A, Genua M, Ghisletti S, Simonatto M, Sabò A, Amati B, Ostuni R§, Natoli G§.
Nat Immunol. 2017 | 10.1038/ni.3710
13. **Inflammatory monocytes hinder antiviral B cell responses.** Sammicheli S, Kuka M, Di Lucia P, de Oya NJ, De Giovanni M, Fioravanti J, Cristofani C, Maganuco CG, Fallet B, Ganzer L, Sironi L, Mainetti M, Ostuni R, Larimore K, Greenberg PD, de la Torre JC, Guidotti LG, Iannacone M.
Sci Immunol. 2016 | 10.1126/sciimmunol.aah6789
14. **Mutual epithelium-macrophage dependency in liver carcinogenesis mediated by ST18.** Ravà M, D'Andrea A, Doni M, Kress TR, Ostuni R, Bianchi V, Morelli MJ, Colin A, Ghisletti S, Nicoli P, Recordati C, Iascone M, Sonzogni A, D'Antiga L, Shukla R, Faulkner GJ, Natoli G, Campaner S, Amati B.
Hepatology. 2017 | 10.1002/hep.28942
15. **TNF-Mediated Restriction of Arginase 1 Expression in Myeloid Cells Triggers Type 2 NO Synthase Activity at the Site of Infection.** Schleicher U, Paduch K, Debus A, Obermeyer S, König T, Kling JC, Ribechini E, Dudziak D, Mougiakakos D, Murray PJ, Ostuni R, Körner H, Bogdan C.
Cell Rep. 2016 | 10.1016/j.celrep.2016.04.001
16. **A dual cis-regulatory code links IRF8 to constitutive and inducible gene expression in macrophages.** Mancino A, Termanini A, Barozzi I, Ghisletti S, Ostuni R, Prosperini E, Ozato K, Natoli G.
Genes Dev. 2015 | 10.1101/gad.257592.114
17. **Chromatin remodelling and autocrine TNFα are required for optimal interleukin-6 expression in activated human neutrophils.** Zimmermann M, Aguilera FB, Castellucci M, Rossato M, Costa S, Lunardi C, Ostuni R, Girolomoni G, Natoli G, Bazzoni F, Tamassia N, Cassatella MA.
Nat Commun. 2015 | 10.1038/ncomms7061
18. **Cutting edge: An inactive chromatin configuration at the IL-10 locus in human neutrophils.** Tamassia N, Zimmermann M, Castellucci M, Ostuni R, Bruderek K, Schilling B, Brandau S, Bazzoni F, Natoli G, Cassatella MA.
J Immunol. 2013 | 10.4049/jimmunol.1203022
19. **Latent enhancers activated by stimulation in differentiated cells.** Ostuni R§*, Piccolo V, * Barozzi I*, Polletti S, * Termanini A, Bonifacio S, Curina A, Prosperini E, Ghisletti S, Natoli G§.
Cell. 2013 | 10.1016/j.cell.2012.12.018
20. **The histone methyltransferase Wbp7 controls macrophage function through GPI glycolipid anchor synthesis.** Austenaa L, Barozzi I, Chronowska A, Termanini A, Ostuni R, Prosperini E, Stewart AF, Testa G, Natoli G.
Immunity. 2012 | 10.1016/j.immuni.2012.02.016
21. **CD14 and NFAT mediate lipopolysaccharide-induced skin edema formation in mice.** Zanoni I*, Ostuni R*, Barresi S, Di Gioia M, Broggi A, Costa B, Marzi R, Granucci F.
J Clin Invest. 2012 | 10.1172/JCI60688
22. **Similarities and differences of innate immune responses elicited by smooth and rough LPS.** Zanoni I, Bodio C, Broggi A, Ostuni R, Caccia M, Collini M, Venkatesh A, Spreafico R, Capuano G, Granucci F.
Immunol Lett. 2012 | 10.1016/j.imlet.2011.12.002
23. **CD14 controls the LPS-induced endocytosis of Toll-like receptor 4.** Zanoni I, Ostuni R, Marek LR, Barresi S, Barbalat R, Barton GM, Granucci F, Kagan JC.
Cell. 2011 | 10.1016/j.cell.2011.09.051
24. **DC-ATLAS: a systems biology resource to dissect receptor specific signal transduction in dendritic cells.** Cavalieri D, Rivero D, Beltrame L, Buschow SI, Calura E, Rizzetto L, Gessani S, Gauzzi MC, Reith W, Baur A, Bonaiuti R, Brandizi M, De Filippo C, D'Oro U, Draghici S, Dunand-Sauthier I, Gatti E, Granucci F, Gündel M, Kramer M, Kuka M, Lanyi A, Melief CJ, van Montfoort N, Ostuni R, Pierre P, Popovici R, Rajnavolgyi E, Schierer S, Schuler G, Soumelis V, Splendiani A, Stefanini I, Torcia MG, Zanoni I, Zollinger R, Figdor CG, Austyn JM.

Immunome Res. 2010 | 10.1186/1745-7580-6-10

25. **CD14 regulates the dendritic cell life cycle after LPS exposure through NFAT activation.** Zanoni I, Ostuni R, Capuano G, Collini M, Caccia M, Ronchi AE, Rocchetti M, Mingozzi F, Foti M, Chirico G, Costa B, Zaza A, Ricciardi-Castagnoli P, Granucci F.
Nature. 2009 | 10.1038/nature08118

REVIEW ARTICLES

1. **Determinants, mechanisms, and functional outcomes of myeloid cell diversity in cancer.** Caronni N, Montaldo E, Mezzanzanica L, Cilenti F, Genua M, Ostuni R§.
Immunol Rev. 2021 | 10.1111/imr.12944
2. **Adaptation and memory in immune responses.** Natoli G§, Ostuni R§.
Nat Immunol. 2019 | 10.1038/s41590-019-0399-9
3. **Heterogeneity of neutrophils.** Ng LG§, Ostuni R§, Hidalgo A§.
Nat Rev Immunol. 2019 | 10.1038/s41577-019-0141-8.
4. **Epigenetic regulation of neutrophil development and function.** Ostuni R§, Natoli G, Cassatella MA, Tamassia N.
Semin Immunol. 2016 | 10.1016/j.smim.2016.04.002
5. **Macrophages and cancer: from mechanisms to therapeutic implications.** Ostuni R§, Kratochvill F, Murray PJ, Natoli G.
Trends Immunol. 2015 | 10.1016/j.it.2015.02.004
6. **Lineages, cell types and functional states: a genomic view.** Ostuni R§, Natoli G.
Curr Opin Cell Biol. 2013 | 10.1016/j.ceb.2013.07.006
7. **Transcriptional control of macrophage diversity and specialization.** Ostuni R, Natoli G.
Eur J Immunol. 2011 | 10.1002/eji.201141706
8. **Deciphering the complexity of Toll-like receptor signaling.** Ostuni R, Zanoni I, Granucci F.
Cell Mol Life Sci. 2010 | 10.1007/s00018-010-0464-x

BOOK CHAPTERS

1. **The control of gene expression in macrophages. "Macrophages: biology and role in the pathology of diseases".** Ostuni R§, Natoli G.
2014 | ISBN 978-1-4939-1310-7
2. **Toll-like Receptors: Structure and Ligand Specificities. "Innate Immunity of the Eye".** 2. Ostuni R, Zanoni I, Granucci F (2013).
2013 | ISBN-10: 935090456X

10 BEST PUBLICATIONS (with narrative)

1) CD14 regulates the dendritic cell life cycle after LPS exposure through NFAT activation.
Nature, 2009 | doi: 10.1038/nature08118.
Zanoni I, ***Ostuni R***, Capuano G, Collini M, Caccia M, Ronchi AE, Rocchetti M, Mingozzi F, Foti M, Chirico G, Costa B, Zaza A, Ricciardi-Castagnoli P, Granucci F.

2) CD14 controls the LPS-induced endocytosis of Toll-like receptor 4.
Cell, 2011 | doi: 10.1016/j.cell.2011.09.051.
Zanoni I, ***Ostuni R***, Marek LR, Barresi S, Barbalat R, Barton GM, Granucci F, Kagan JC.

3) CD14 and NFAT mediate lipopolysaccharide-induced skin edema formation in mice.
Journal of Clinical Investigation, 2012 | doi: 10.1172/JCI60688.
Zanoni I*, ***Ostuni R****, Barresi S, Di Gioia M, Broggi A, Costa B, Marzi R, Granucci F.

As a graduate student, I contributed to establish CD14 — a co-receptor for lipopolysaccharide (LPS) — as a key organizer of inflammatory responses in innate immune cells. We discovered a CD14-dependent pathway in dendritic cells exposed to LPS, which led to calcium signaling and NFAT activation. We then showed that CD14 regulates endosomal translocation of TLR4 and downstream IFN I production in LPS-activated macrophages and dendritic cells. These papers are important because they reveal mechanistic determinants of inflammatory responses at the interface of signal transduction and cell biology.

4) Latent enhancers activated by stimulation in differentiated cells
Cell, 2013 | doi: 10.1016/j.cell.2012.12.018
Ostuni R§, Piccolo V, Barozzi I, Polletti, Termanini A, Bonifacio S, Curina A, Prosperini E, Ghisletti S, Natoli G§.

As a postdoctoral fellow, I pioneered the use of genomics to decipher regulatory principles of inflammatory gene expression. Here, I discovered latent enhancers, a class of genomic elements controlling short-term transcriptional and epigenetic memory in differentiated macrophages. These findings challenged the dogmas that the epigenomic repertoire of cells is only set during development. Latent enhancers are now recognized as drivers of trained immunity and plasticity in macrophages.

5) Opposing macrophage polarization programs show extensive epigenomic and transcriptional cross-talk
Nature Immunology, 2017 | doi: 10.1038/ni.3710
Piccolo V, Curina A, Genua M, Ghisletti S, Simonatto M, Sabò A, Amati B, ***Ostuni R***§, Natoli G§.

6) Adaptation and memory in immune responses.
Nature Immunology, 2019 | doi: 10.1038/s41590-019-0399-9.
Natoli G§, ***Ostuni R***§.

As a Group Leader, I elucidated principles of signal integration that underlie macrophage responses to mixed stimulations within a complex microenvironment. Using IFN-γ and IL-4 as paradigmatic cytokines, we found that antagonistic biological programs can to a large extent co-exist in macrophages. On the other hand, costimulation with the two cytokines resulted in reciprocal inhibitory effects at a specific set of enhancers. These studies highlight chromatin as a platform for the integration of antagonistic signals that control macrophage activities in complex environments.

7) A PGE_2-MEF2A axis enables context-dependent control of inflammatory gene expression
Immunity, 2021 | doi: 10.1016/j.immuni.2021.05.016
Cilenti F, Barbiera G, Caronni N, Iodice D, Montaldo E, Barresi S, Lusito E, Cuzzola V, Vittoria FM, Mezzanzanica L, Miotto P, Di Lucia P, Lazarevic D, Cirillo DM, Iannacone M, Genua M, ***Ostuni R***§.

The identification of the PGE_2-MEF2A axis in macrophages **is my major achievement so far**. We found that PGE2, a potent immune modulatory signal capable of suppressing IFN I expression in macrophages, acts upon a set of inflammatory gene enhancers marked by the transcription factor MEF2A. Deletion of MEF2A phenocopied PGE2 treatment and abolished IFN I induction upon exposure to multiple innate immune stimuli or live pathogens. Mechanistically, PGE2 interfered with LPS-mediated activation of ERK5, a transcriptional partner of MEF2. This study uncovers a novel

immune modulatory activity of PGE2 and highlights a transcriptional circuit for IFN I induction with relevance for the treatment of infectious diseases or cancer. This discovery provides theoretical and experimental support to the development of approaches that manipulate inflammation for cancer immunotherapy.

8) Heterogeneity of neutrophils.
Nature Reviews Immunology, 2019 | doi: 10.1038/s41577-019-0141-8
Ng LG[§], ***Ostuni R***[§], Hidalgo A[§].

9) Co-option of Neutrophil Fates by Tissue Environments.
Cell, 2020 | doi: 10.1016/j.cell.2020.10.003
Ballesteros I, Rubio-Ponce A, Genua M, Lusito E, Kwok I, Fernández-Calvo G, Khoyratty TE, van Grinsven E, González-Hernández S, Nicolás-Ávila JÁ, Vicanolo T, Maccataio A, Benguría A, Li JL, Adrover JM, Aroca-Crevillen A, Quintana JA, Martín-Salamanca S, Mayo F, Ascher S, Barbiera G, Soehnlein O, Gunzer M, Ginhoux F, Sánchez-Cabo F, Nistal-Villán E, Schulz C, Dopazo A, Reinhardt C, Udalova IA, Ng LG, ***Ostuni R***, Hidalgo A.

10) Cellular and transcriptional dynamics of human neutrophils at steady state and upon stress
under revision at Nature Immunology
Montaldo E[§], Lusito E, Bianchessi V, Scala S, Basso-Ricci L, Cantaffa C, Masserdotti A, Barilaro M, Barresi S, Genua M, Barbiera G, Lazarevic D, Messina C, Xue E, Marktel S, Tresoldi C, Milani R, Ronchi P, Gattillo S, Santoleri L, Ditadi A, Belfiori G, Aleotti F, Naldini MM, Gentner B, Hidalgo A, Kwok I, Ng LG, Crippa S, Falconi M, Naldini L, Ciceri F, Aiuti A, ***Ostuni R***[§].

Neutrophils are often viewed as poorly plastic, but evidence suggest they are functionally diverse. In this context, we proposed that transcriptional and chromatin dynamics underlie neutrophil heterogeneity, and then validated this hypothesis by defining tissue-specific phenotypic, molecular, and functional programs of mouse neutrophils. Diversification mechanisms of neutrophil behaviors may shape organ homeostasis, as well as contribute to pathology. In a study under revision at Nature Immunology, we report a comprehensive immunophenotypic and transcriptome analysis, at bulk and single-cell level, of neutrophils from healthy donors and patients undergoing stress myelopoiesis upon exposure to growth factors, transplantation of hematopoietic stem cells (HSC-T), or development of pancreatic cancer. We found an extreme diversity of human neutrophils in vivo, which reflected the rates of cell mobilization, differentiation, and exposure to environmental signals. Integrated control of developmental and inducible transcriptional programs linked flexible granulopoietic outputs with elicitation of context-dependent functional responses. In this context, we detected an acute interferon (IFN) response in the blood of HSC-T patients that was mirrored by marked upregulation of IFN-stimulated genes in neutrophils but not in monocytes. Systematic characterization of human neutrophil plasticity may uncover clinically relevant biomarkers and support the development of diagnostic and therapeutic tools.