BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Alessandra Renieri	Full Professor of Medical Genetics University of Siena, Siena, Italy Director of Medical Genetics Unit Azienda Ospedaliera Universitaria Senese, Siena, Italy

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE		INSTITUTION AND LOCATION
University of Siena, Italy	M.D.	06/89	School of Medicine
University of Turin, Italy	Ph.D.	06/94	Human Genetics
University of Florence, Italy	Specialty	11/98	Medical Genetics
Baylor College of Medicine, Houston, Texas, USA	-	10/93	Molecular Genetics

A. Personal Statement

Alessandra Renieri graduated in Medicine at the University of Siena and obtained a PhD in Human Genetics at the University of Torino. Subsequently she received a specialist degree in Medical Genetics at the University of Florence and she then went back to Siena where she worked first as Medical Assistant and then as researcher. In 2000 she was appointed Associate Professor and from 2007 she is **Full Professor of Medical Genetics** at the School of Medicine of the University of Siena. From July 1st, 2019 she is member of the Committee for Advanced Therapies (CAT) at the European Medicines Agency.

From 1992 to 2002 she personally performed 1240 second-level genetic counselling activities at the division of Medical Genetics of Siena, which imply identifying a case on the basis of clinical genetics, recommending a possible molecular diagnosis, coordinating the implementation of the research, assessing the recurrence risk for relatives and, sometimes, making pre-symptomatic diagnosis. She is the director of the Medical Genetics Unit of the General Hospital of Siena. Since 2001 she has coordinated, as director of the Medical Genetics Unit, more than 10,000 genetic counselling.

Her main research interest has always been the study of the **genetic basis of rare diseases**, with a special focus on Rett syndrome, and other conditions with intellectual disabilities (ID), Alport syndrome, retinoblastoma and other rare cancers. She identified two new genes disease: FACL4 gene for X-linked ID and FOXG1 gene for Rett syndrome. Her laboratory was among the first in Italy to introduce the technology of array-CGH and of Next Generation Sequencing (NGS) for clinical diagnosis.

She has been involved in research on **Rett syndrome** for many years and she contributed to the identification of all 3 known genes presently associated to the disease, as well as to the definition of the associated clinical phenotype. Her group identified FOXG1 as the first autosomal gene involved in Rett syndrome. Her laboratory is a referral center for Rett in Italy and, since 1998, she directs the Genetic Biobank of Siena (GBS, http://www.biobank.unisi.it), one of the few in Italy certified SIGU-CERT and ISO9001, and funded by Telethon since 2002. GBS is the Italian Partner of BBMRI (Biobanking and Biomolecular Resources Research Infrastructure), member of EuroBioBank and RD-Connect. Since 2009, she coordinates the international Rett database network (http://www.rettdatabasenetwork.org). She also coordinates the Italian Registry of **Alport disease**, an Italian network for Alport disease, which aims to fund and support actions in favour of the management and treatment of ATS patients. In order to create a human cellular model for the study of the pathogenic mechanisms of Rett syndrome directly in human affected neurons, she set up the technique of genetic reprogramming in her laboratory (iPS).

She has been involved in **cancer genetics** for many years, including retinoblastoma, breast, colon and lung cancer. Her laboratory is among the first in Italy to introduce the use of NGS for “liquid biopsy” as an innovative diagnostic and prognostic technique in cancer for early detection and monitoring cancer growth and resistance to treatment for “personalized medicine”.

Prof. Renieri is HCP (Health Care Provider) representative/sub-representative for Azienda Ospedaliera Universitaria Senese (AOUS) of 5 **European Reference Networks** (ERNs): EuroBloodNet (on rare haematological diseases); ERKNET (on rare kidney diseases); ERN ITHACA (on ID and congenital anomalies); PaedCan-ERN (on paediatric cancers) and EURACAN (for rare adult solid cancers). She is coordinator of Registry WP with the ERN ITHACA and involved in the interoperability between Registries at European Level (coordinator of Rett Networked Database) and is leading for ERN ITHACA the project for H2020 HP-PJ-06-2016 "Support for New Registries" call.

She is an active member of the Telethon Network of Genetic Biobanks. She acts a medical advisor with several patient organizations including AIRETT, and supervises specialist clinics for rare disorders within AOUS.

Since 2017 her reasearch interest is focused on **gene editing** using CRISPR systems and its translation to clinical practice. Currently, she is running four gene editing projects. Three are using Crispr/Cas9 and AAV system and are related to Rett syndrome (FOXG1 variant), Parkinson (LRRK2 and GBA) and Alport syndrome (COL4A5). One is using Crispr/Cpf1 and lentiviral vector and it is related to Chronic Lymphocytic Leukemia and other TP53 mutared cancers. More recently, in Siena she was sorting out a sort of “factory” for producing plasmid & vectors for gene editing in vitro & animal models, preliminary for clinical trial for a number of diseases including Rett syndrome, Parkinson disease, Alport syndrome and Pompe diseases, among others.

To rapidly respond to the ongoing COVID-19 pandemic, she is focusing on developing the most informative diagnostic test and the most powerful therapy on the basis of host genome. She is leading the *GEN-COVID* Multicenter Study aimed at enrolling 2,000 COVID-19 patients for host genetic analysis and she is member e co-founder of the international Host Genetic Initiative (HGI). For these purposes, recently, a section dedicated to COVID-19 was included in the established and certified Biobank and Registry of the Medical Genetics Unit of the Hospital. The *Genetic and COVID-19 Biobank of Siena*, is member of BBMRI-IT, of Telethon Network of Genetic Biobanks (project no. GTB18001), of EuroBioBank, and of D-Connect, provided us with specimens.

Research activities of Prof. Alessandra Renieri are substantiated by 293 original publications with a total IF > 1000 and 3 patents. She is author of 6 book chapters, 9 reviews made by request, and one N&V in Nat Genet.

Citation parameters (Scopus– update December 2021):

N publications in the last 10ys: 182
N total citations: 13013
H-index: 55
average citations per item: 39,43

Prof. Alessandra Renieri ranks above the median for full professors according to ANVUR scientific quality parameters (contemporary H –index, number of publications in the last ten years, normalized citations). Being also over the median for total H-index and total citations numbers, she has been recently selected in the committee for National Scientific Qualification (2012-2015).

B. Positions and Honours

Positions and employment

1993-1998 - Medical Assistant - Medical Genetics, Hospital of Siena, Italy
1998-2000 - Researcher - Medical Genetics, School of Medicine, University of Siena, Italy

2000-2007 - Associate Professor - Medical Genetics, School of Medicine, University of Siena, Italy
Since 2002 - Director of the Medical Genetics division, Hospital of Siena, Italy
Since 2003 - Director of the Specialty School of Medical Genetics, University of Siena, Italy
2001-2004 - Coordinator of the Research Doctorate of Medical Genetics, University of Siena
Since 2005 - Director of the PhD School in Oncology and Genetics, University of Siena, Italy, that becomes in 2011 Doctorate in Genetics, Oncology and Clinical Medicine (GenOMeC)
Since 2006 - Coordinator of the inter-University Master in "Clinical Genetics".
Since 2007 - Full Professor - Medical Genetics, University of Siena, Italy
2015-2019 - Director of the PhD School in Doctorate in Genetics, Oncology and Clinical Medicine (GenOMeC), University of Siena, Italy.

Other experiences and affiliations to scientific societies

1989-1993	Research experience at Medical Genetics laboratory, University of Siena
1993	Research experience at Molecular Genetics laboratory (Prof. A. Ballabio), Baylor College of Medicine, Houston, Texas, USA
Since 1991	Clinical experience as coordinator of about 1900 molecular diagnoses (index cases) of 15 different monogenic diseases, Medical Genetics, University of Siena.
Since 1992	Clinical experience in Genetic Counseling (about 1240 sessions) at the Medical Genetics, University of Siena.
Since 1991	Affiliated to Italian Society of Human Genetics (SIGU) (before AIGM)
Since 1993	Affiliated to American Society of Human genetics (ASHG)
Since 1993	Affiliated to European Society of Human genetics (ESHG)
Since 1999	Teaching Medical Genetics in the School of Medicine, Siena
2002 & 2004	Wellcome Trust grants reviewer
2004-2009	Board member of European Society of Human genetics (ESHG)
Since 2013	SIGU representative within UEMS (Union Européenne des Médecins Spécialistes - European Union of Medical Specialists)
Since 2014	Affiliated to EBMG (European Board of Medical Genetics), a professional organism of ESHG
Since 2014	Section Editor di European Journal of Human Genetics (EJHG)
Since 2014	Coordinator of the Working Group of Clinical Genetics of the SIGU
Since 2016	Member of Ethical Committee of Azienda Ospedaliera Universitaria Senese, Siena, Italy
Since 2017	Secretary of Clinical Genetics Section within UEMS (Union Européenne des Médecins Spécialistes - European Union of Medical Specialists)
2017	Coordinator of Network for Italian Genomes (NIG)
Since 2019	Member of The Committee for Advanced Therapies (CAT) of the EMA (European Medicines Agency).

Patent

- Alessandra Renieri e Ilaria Meloni "Diagnostic and therapeutic tools for X-linked mental retardation syndrome " International application N° PCT/IT03/00134 emesso nel marzo 2003 e pubblicato il16 giugno 2005 AS UD-2005-0130162-A1.
- Renieri A, Conticello S, Pinto AM, Meloni I, Daga S, Donati F, Croci S, Lopergolo D. "CRISPR-Cas system for gene therapy" (Patent application N° 102018000020230) for the use of CRISPR/Cas9 technology in rare genetic diseases. December 19, 2018.

- Renieri A, Conticello S, Donati F, Niccheri F, Mari F, Papa FT, Lorenzetti FC. “Sistema CRISPR-Cas per l’editing genomico” (Patent application N° 102018000009431) for the employment of CRISPR/Cpf1 technology for specific delivery of suicide gene in cancer cells mutated in TP53. October 15, 2018.

Selected recent relevant peer-reviewed publications

1. Fallerini C, Picchiotti N, Baldassarri M, Zguro K, Daga S, Fava F, Benetti E, Amitrano S, Bruttini M, Palmieri M, Croci S, Lista M, Beligni G, Valentino F, Meloni I, Tanfoni M, Minnai F, Colombo F, Cabri E, Fratelli M, Gabbi C, Mantovani S, Frullanti E, Gori M, Crawley FP, Butler-Laporte G, Richards B, Zeberg H, Lipcsey M, Hultström M, Ludwig KU, Schulte EC, Pairo-Castineira E, Baillie JK, Schmidt A, Frithiof R; WES/WGS Working Group Within the HGI; GenOMICC Consortium; GEN-COVID Multicenter Study, Mari F, Renieri A, Furini S. Common, low-frequency, rare, and ultra-rare coding variants contribute to COVID-19 severity. Hum Genet. 2021 Dec 10. doi: 10.1007/s00439-021-02397-7. Epub ahead of print. PMID: 34889978.
2. Pairo-Castineira E, Clohisey S, Klaric L, Bretherick AD, Rawlik K, Pasko D, Walker S, Parkinson N, Fourman MH, Russell CD, Furniss J, Richmond A, Gountouna E, Wrobel N, Harrison D, Wang B, Wu Y, Meynert A, Griffiths F, Oosthuyzen W, Kousathanas A, Moutsianas L, Yang Z, Zhai R, Zheng C, Grimes G, Beale R, Millar J, Shih B, Keating S, Zechner M, Haley C, Porteous DJ, Hayward C, Yang J, Knight J, Summers C, Shankar-Hari M, Klenerman P, Turtle L, Ho A, Moore SC, Hinds C, Horby P, Nichol A, Maslove D, Ling L, McAuley D, Montgomery H, Walsh T, Pereira AC, Renieri A; GenOMICC Investigators; ISARIC4C Investigators; COVID-19 Human Genetics Initiative; 23andMe Investigators; BRACOVID Investigators; Gen-COVID Investigators, Shen X, Ponting CP, Fawkes A, Tenesa A, Caulfield M, Scott R, Rowan K, Murphy L, Openshaw PJM, Semple MG, Law A, Vitart V, Wilson JF, Baillie JK. Genetic mechanisms of critical illness in COVID-19. Nature. 2021; 591(7848):92-98. doi: 10.1038/s41586-020-03065-y.. PMID: 33307546.
3. Zhang Q, Bastard P, Liu Z, Le Pen J, Moncada-Velez M, Chen J, Ogishi M, Sabli IKD, Hodeib S, Korol C, Rosain J, Bilguvar K, Ye J, Bolze A, Bigio B, Yang R, Arias AA, Zhou Q, Zhang Y, Onodi F, Korniotis S, Karpf L, Philippot Q, Chbihi M, Bonnet-Madin L, Dorgham K, Smith N, Schneider WM, Razooky BS, Hoffmann HH, Michailidis E, Moens L, Han JE, Lorenzo L, Bizien L, Meade P, Neehus AL, Ugurbil AC, Corneau A, Kerner G, Zhang P, Rapaport F, Seeleuthner Y, Manry J, Masson C, Schmitt Y, Schlüter A, Le Voyer T, Khan T, Li J, Fellay J, Roussel L, Shahrooei M, Alosaimi MF, Mansouri D, Al-Saud H, Al-Mulla F, Almourfi F, Al-Muhsen SZ, Alsohime F, Al Turki S, Hasanato R, van de Beek D, Biondi A, Bettini LR, D'Angio' M, Bonfanti P, Imberti L, Sottini A, Paghera S, Quiros-Roldan E, Rossi C, Oler AJ, Tompkins MF, Alba C, Vandernoot I, Goffard JC, Smits G, Migeotte I, Haerynck F, Soler-Palacin P, Martin-Nalda A, Colobran R, Morange PE, Keles S, Çölkesen F, Ozcelik T, Yasar KK, Senoglu S, Karabela ŞN, Rodríguez-Gallego C, Novelli G, Hraiech S, Tandjaoui-Lambiotte Y, Duval X, Laouénan C; COVID-STORM Clinicians; COVID Clinicians; Imagine COVID Group; French COVID Cohort Study Group; CoV-Contact Cohort; Amsterdam UMC Covid-19 Biobank; COVID Human Genetic Effort; NIAID-USUHS/TAGC COVID Immunity Group, Snow AL, Dalgard CL, Milner JD, Vinh DC, Mogensen TH, Marr N, Spaan AN, Boisson B, Boisson-Dupuis S, Bustamante J, Puel A, Ciancanelli MJ, Meyts I, Maniatis T, Soumelis V, Amara A, Nussenzweig M, García-Sastre A, Krammer F, Pujol A, Duffy D, Lifton RP, Zhang SY, Gorochov G, Béziat V, Jouanguy E, Sancho-Shimizu V, Rice CM, Abel L, Notarangelo LD, Cobat A, Su HC, Casanova JL. Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. Science. 2020 Oct 23;370(6515):eabd4570. doi: 10.1126/science.abd4570. Epub 2020 Sep 24. PMID: 32972995; PMCID: PMC7857407. As part of GEN-COVID consortium.

4. Fallerini C, Daga S, Benetti E, Picchiotti N, Zguro K, Catapano F, Baroni V, Lanini S, Bucalossi A, Marotta G, Colombo F, Baldassarri M, Fava F, Beligni G, Di Sarno L, Alaverdian D, Palmieri M, Croci S, Isidori AM, Furini S, Frullanti E; GEN-COVID Multicenter Study, Renieri A, Mari F. SELP Asp603Asn and severe thrombosis in COVID-19 males. J Hematol Oncol. 2021 Aug 16;14(1):123. doi: 10.1186/s13045-021-01136-9. PMID: 34399825; PMCID: PMC8365289.

5. Benetti E, Tita R, Spiga O, Ciolfi A, Birolo G, Bruselles A, Doddato G, Giliberti A, Marconi C, Musacchia F, Pippucci T, Torella A, Trezza A, Valentino F, Baldassarri M, Brusco A, Asselta R, Bruttini M, Furini S, Seri M, Nigro V, Matullo G, Tartaglia M, Mari F; GEN-COVID Multicenter Study, Renieri A, Pinto AM. ACE2 gene variants may underlie interindividual variability and susceptibility to COVID-19 in the Italian population. Eur J Hum Genet. 2020 Nov;28(11):1602-1614. doi: 10.1038/s41431-020-0691-z. Epub 2020 Jul 17. PMID: 32681121; PMCID: PMC7366459.

6. Benetti E, Giliberti A, Emiliozzi A, Valentino F, Bergantini L, Fallerini C, Anedda F, Amitrano S, Conticini E, Tita R, d'Alessandro M, Fava F, Marcantonio S, Baldassarri M, Bruttini M, Mazzei MA, Montagnani F, Mandalà M, Bargagli E, Furini S; GEN-COVID Multicenter Study, Renieri A, Mari F. Clinical and molecular characterization of COVID-19 hospitalized patients. PLoS One. 2020 Nov 18;15(11):e0242534. doi: 10.1371/journal.pone.0242534. PMID: 33206719; PMCID: PMC7673557.

7. Butler-Laporte G, Nakanishi T, Mooser V, Renieri A, Amitrano S, Zhou S, Chen Y, Forgetta V, Richards JB. The effect of angiotensin-converting enzyme levels on COVID-19 susceptibility and severity: a Mendelian randomization study. Int J Epidemiol. 2021 Mar 3;50(1):75-86. doi: 10.1093/ije/dyaa229. PMID: 33349849; PMCID: PMC7799043.

8. Daga S, Fallerini C, Baldassarri M, Fava F, Valentino F, Doddato G, Benetti E, Furini S, Giliberti A, Tita R, Amitrano S, Bruttini M, Meloni I, Pinto AM, Raimondi F, Stella A, Biscarini F, Picchiotti N, Gori M, Pinoli P, Ceri S, Sanarico M, Crawley FP, Birolo G; GEN-COVID Multicenter Study, Renieri A, Mari F, Frullanti E. Employing a systematic approach to biobanking and analyzing clinical and genetic data for advancing COVID-19 research. Eur J Hum Genet. 2021 May;29(5):745-759. doi: 10.1038/s41431-020-00793-7. Epub 2021 Jan 17. PMID: 33456056; PMCID: PMC7811682.

9. Daga S, Fallerini C, Baldassarri M, Fava F, Valentino F, Doddato G, Benetti E, Furini S, Giliberti A, Tita R, Amitrano S, Bruttini M, Meloni I, Pinto AM, Raimondi F, Stella A, Biscarini F, Picchiotti N, Gori M, Pinoli P, Ceri S, Sanarico M, Crawley FP, Birolo G; GEN-COVID Multicenter Study, Renieri A, Mari F, Frullanti E. Employing a systematic approach to biobanking and analyzing clinical and genetic data for advancing COVID-19 research. Eur J Hum Genet. 2021 May;29(5):745-759. doi: 10.1038/s41431-020-00793-7. Epub 2021 Jan 17. PMID: 33456056; PMCID: PMC7811682.

10. Butler-Laporte G, Nakanishi T, Mooser V, Morrison DR, Abdullah T, Adeleye O, Mamlouk N, Kimchi N, Afrasiabi Z, Rezk N, Giliberti A, Renieri A, Chen Y, Zhou S, Forgetta V, Richards JB. Vitamin D and COVID-19 susceptibility and severity in the COVID-19 Host Genetics Initiative: A Mendelian randomization study. PLoS Med. 2021 Jun 1;18(6):e1003605. doi: 10.1371/journal.pmed.1003605. PMID: 34061844; PMCID: PMC8168855.

11. Monticelli M, Hay Mele B, Benetti E, Fallerini C, Baldassarri M, Furini S, Frullanti E, Mari F, Andreotti G, Cubellis MV, Renieri A; Gen-Covid Multicenter Study. Protective Role of a *TMPRSS2* Variant on Severe COVID-19 Outcome in Young Males and Elderly Women. Genes (Basel). 2021 Apr 19;12(4):596. doi: 10.3390/genes12040596. PMID: 33921689; PMCID: PMC8073081.

12. Nakanishi T, Pigazzini S, Degenhardt F, Cordioli M, Butler-Laporte G, Maya-Miles D, Nafría-Jiménez B, Bouysran Y, Niemi M, Palom A, Ellinghaus D, Khan A, Martínez-Bueno M, Rolker S, Amitano S, Tato LR;

FinnGen; COVID-19 Host Genetics Initiative, Fava F, Spinner CD, Prati D, Bernardo D, Garcia F, Darcis G, Fernández-Cadenas I, Holter JC, Banales J, Frithiof R, Kiryluk K, Duga S, Asselta R, Pereira AC, Romero-Gómez M, Bujanda L, Hov JR, Migeotte I, Renieri A, Planas AM, Ludwig KU, Buti M, Rahmouni S, Alarcón-Riquelme ME, Schulte EC, Franke A, Karlsen TH, Valenti L, Zeberg H, Richards JB, Ganna A. Age-dependent impact of the major common genetic risk factor for COVID-19 on severity and mortality. medRxiv [Preprint]. 2021 Mar 12:2021.03.07.21252875. doi: 10.1101/2021.03.07.21252875. PMID: 33758887; PMCID: PMC7987046.

13. Zhang S, Cooper-Knock J, Weimer AK, Harvey C, Julian TH, Wang C, Li J, Furini S, Frullanti E, Fava F, Renieri A, Pan C, Song J, Billing-Ross P, Gao P, Shen X, Timpanaro IS, Kenna KP; VA Million Veteran Program; GEN-COVID Network, Davis MM, Tsao PS, Snyder MP. Common and rare variant analyses combined with single-cell multiomics reveal cell-type-specific molecular mechanisms of COVID-19 severity. medRxiv [Preprint]. 2021 Jun 21:2021.06.15.21258703. doi: 10.1101/2021.06.15.21258703. PMID: 34189540; PMCID: PMC8240695.

14. Fallerini C, Daga S, Mantovani S, Benetti E, Picchiotti N, Francisci D, Paciosi F, Schiaroli E, Baldassarri M, Fava F, Palmieri M, Ludovisi S, Castelli F, Quiros-Roldan E, Vaghi M, Rusconi S, Siano M, Bandini M, Spiga O, Capitani K, Furini S, Mari F; GEN-COVID Multicenter Study, Renieri A, Mondelli MU, Frullanti E. Association of Toll-like receptor 7 variants with life-threatening COVID-19 disease in males: findings from a nested case-control study. Elife. 2021 Mar 2;10:e67569. doi: 10.7554/eLife.67569. PMID: 33650967; PMCID: PMC7987337.

15. Baldassarri M, Fava F, Fallerini C, Daga S, Benetti E, Zguro K, Amitrano S, Valentino F, Doddato G, Giliberti A, Di Sarno L, Palmieri M, Carriero ML, Alaverdian D, Beligni G, Iuso N, Castelli F, Quiros-Roldan E, Mondelli MU, Miceli R, Frullanti E, Furini S, Mari F, Renieri A, Gabbi C, On Behalf Of The Gen-Covid Multicenter Study. Severe COVID-19 in Hospitalized Carriers of Single *CFTR*Pathogenic Variants. J Pers Med. 2021 Jun 15;11(6):558. doi: 10.3390/jpm11060558. PMID: 34203982; PMCID: PMC8232773

16. Zanella I, Zacchi E, Piva S, Filosto M, Beligni G, Alaverdian D, Amitrano S, Fava F, Baldassarri M, Frullanti E, Meloni I, Renieri A; GEN-COVID Multicenter Study; GEVACOBA Study Group, Castelli F, Quiros-Roldan E. *C9orf72*Intermediate Repeats Confer Genetic Risk for Severe COVID-19 Pneumonia Independently of Age. Int J Mol Sci. 2021 Jun 29;22(13):6991. doi: 10.3390/ijms22136991. PMID: 34209673; PMCID: PMC8268051.

17. Baldassarri M, Picchiotti N, Fava F, Fallerini C, Benetti E, Daga S, Valentino F, Doddato G, Furini S, Giliberti A, Tita R, Amitrano S, Bruttini M, Croci S, Meloni I, Pinto AM, Iuso N, Gabbi C, Sciarra F, Venneri MA, Gori M, Sanarico M, Crawley FP, Pagotto U, Fanelli F, Mezzullo M, Dominguez-Garrido E, Planas-Serra L, Schlüter A, Colobran R, Soler-Palacin P, Lapunzina P, Tenorio J, Pujol A, Castagna MG, Marcelli M, Isidori AM, Renieri A, Frullanti E, Mari F; Spanish Covid HGE, GEN-COVID Multicenter Study. Shorter androgen receptor polyQ alleles protect against life-threatening COVID-19 disease in European males. EBioMedicine. 2021 Mar;65:103246. doi: 10.1016/j.ebiom.2021.103246. Epub 2021 Feb 26. PMID: 33647767; PMCID: PMC7908850.