






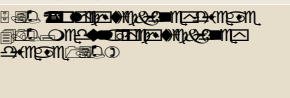



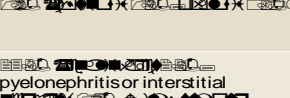


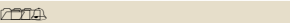
Sindrome nefrosica steroideo-resistente:

diagnostica

Paola Romagnani

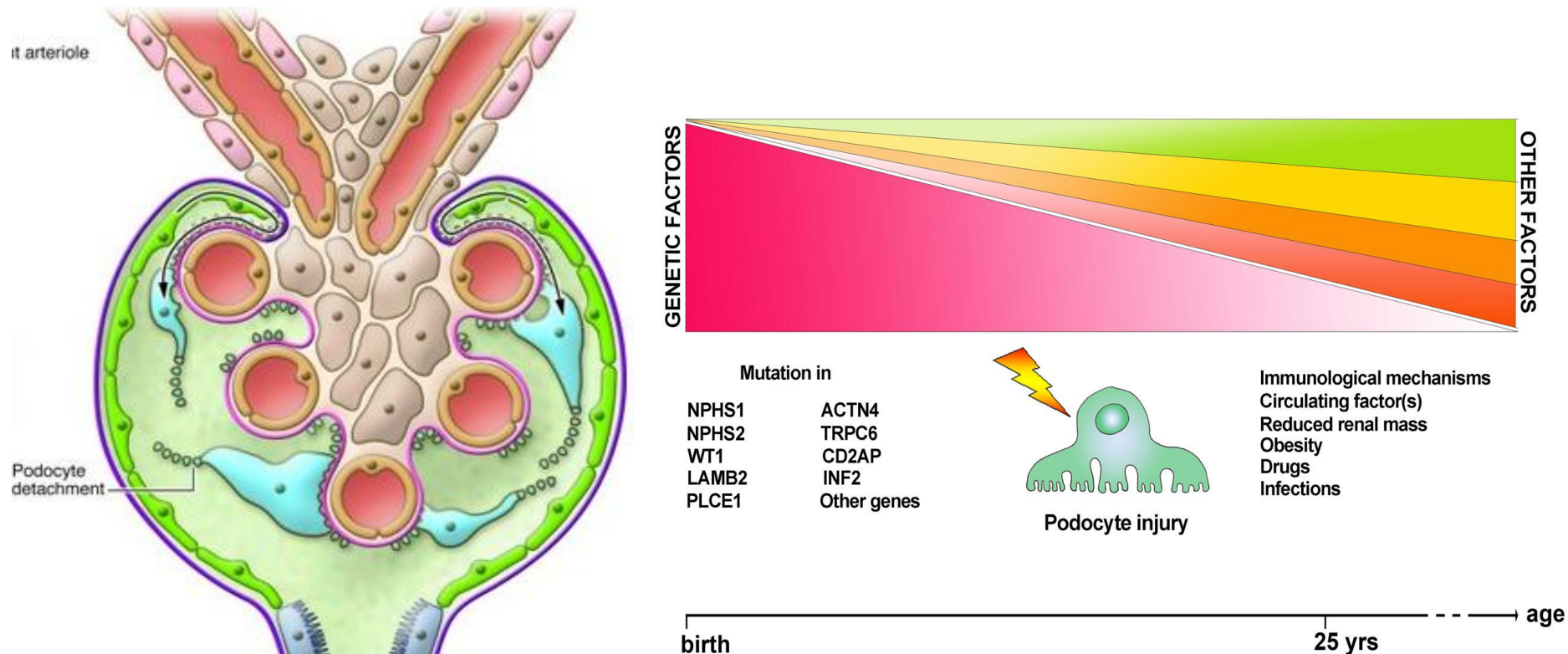


Elevata prevalenza di cause genetiche nelle malattie renali croniche che esordiscono nell'infanzia

Diagnostic group	Indication to run a gene panel	Proportion of cases of early-onset CKD	Number of known causative genes	Percentage of cases caused by known genes (multiplied by fraction of all CKD)	Refs
CAKUT	CAKUT evident by renal imaging		82	"82% 25000"	29276 1484
SRNS	SRNS		16	"16% 25000"	19442
 Evidence of proteinuria and haematuria	Evidence of proteinuria and haematuria		27	"27% 25000"	4
Renal cystic ciliopathies	Increased echogenicity on renal ultrasound 		95	"95% 25000"	11875 8522
aHUS	 and AKI		9	"9% 25000"	8666
Nephrolithiasis or nephrocalcinosis	 disease or nephrocalcinosis		13	"13% 25000"	4594
Other	Other indications of genetic disease pyelonephritis or interstitial 		209	"209% 25000"	Not available
Total	—		~219	"219% 25000"	—

Ogni singolo gene è raro ma i geni che possono causarla sono tanti.....

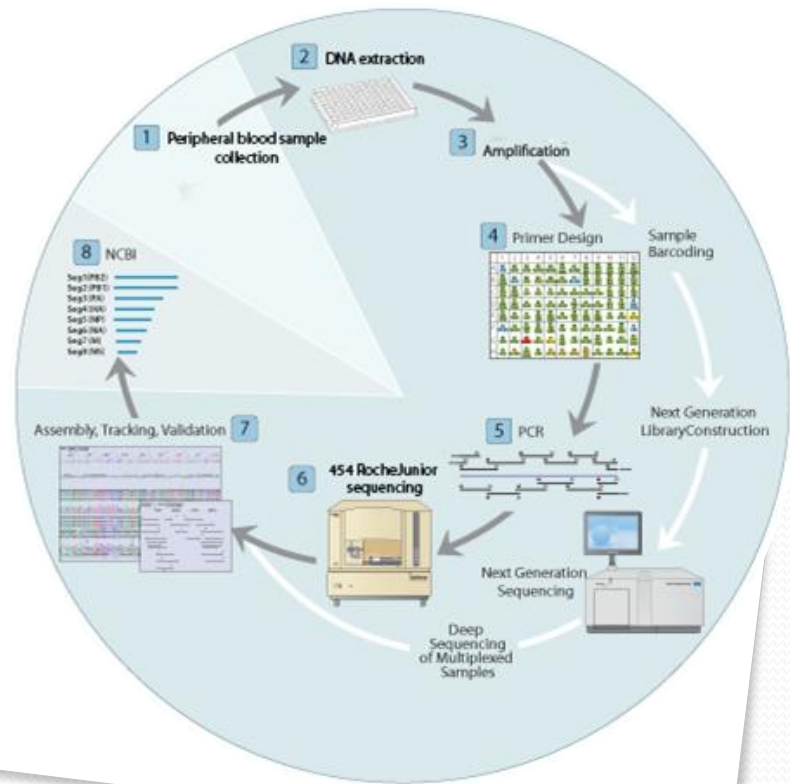
Le cause della sindrome nefrosica steroido-resistente risiedono in alterazioni della barriera di filtrazione glomerulare, soprattutto nelle cellule che ne rappresenta il costituente fondamentale, il podocita



Le nuove tecniche genetiche di sequenziamento esteso consentono di analizzare molti geni nello stessa analisi

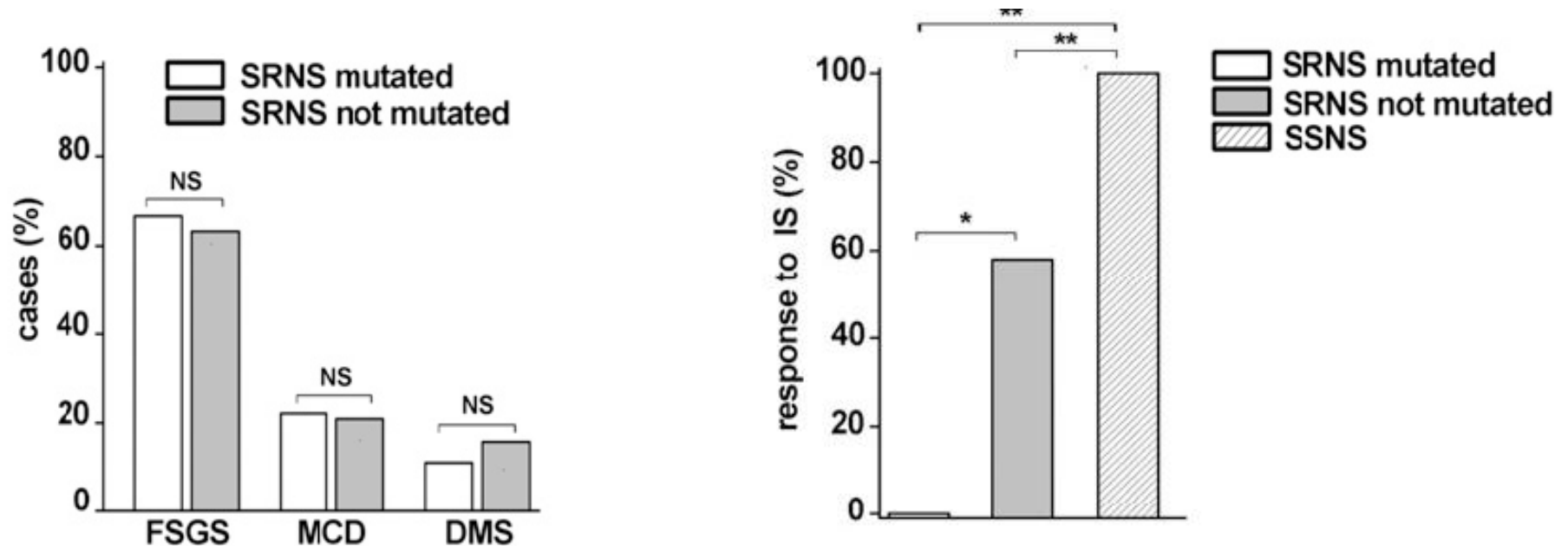
Circa il 30% dei bambini affetti da sindrome nefrosica hanno una alterazione genetica in un gene coinvolto nel mantenimento della struttura del podocita

2013-2014



Heterogeneous Genetic Alterations in Sporadic Nephrotic Syndrome Associate with Resistance to Immunosuppression

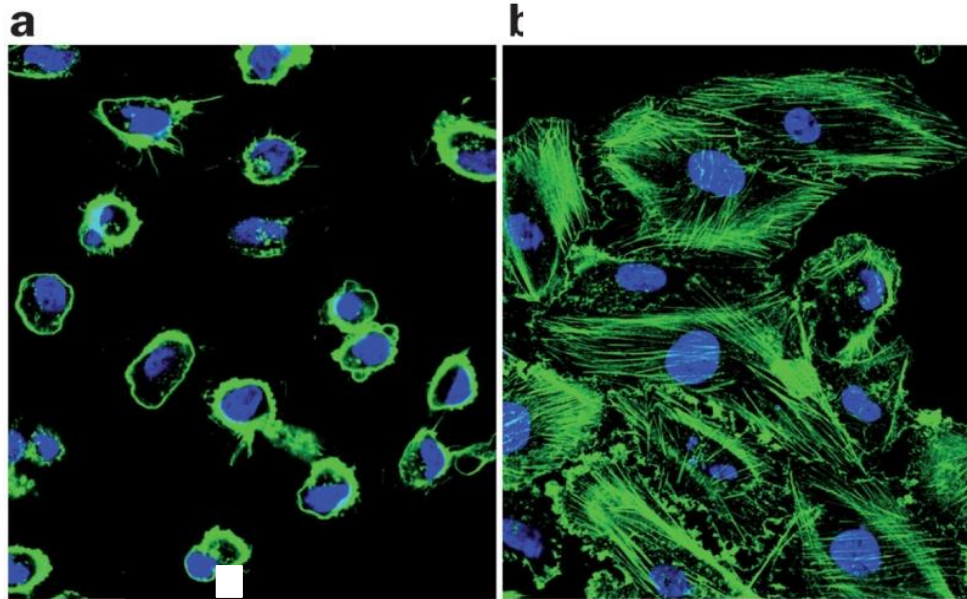
Sabrina Giglio,^{*,†} Aldesia Provenzano,^{*} Benedetta Mazzinghi,[†] Francesca Becherucci,[‡] Laura Giunti,[†] Giulia Sansavini,[‡] Fiammetta Ravaglia,[‡] Rosa Maria Roperto,[‡] Silvia Farsetti,[‡] Elisa Benetti,[§] Mario Rotondi,^{||} Luisa Murer,[§] Elena Lazzeri,[¶] Laura Lasagni,[¶] Marco Materassi,[‡] and Paola Romagnani^{*,‡¶}



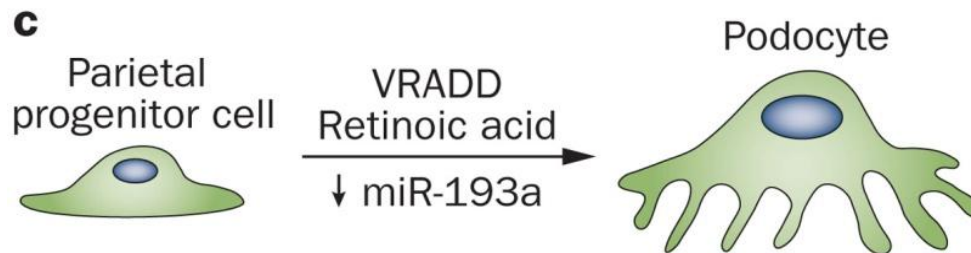
Alcuni pazienti portano varianti genetiche di significato incerto



E' possibile però studiarle raccogliendo dalle urine del bambino affetto progenitori renali e facendoli diventare podociti



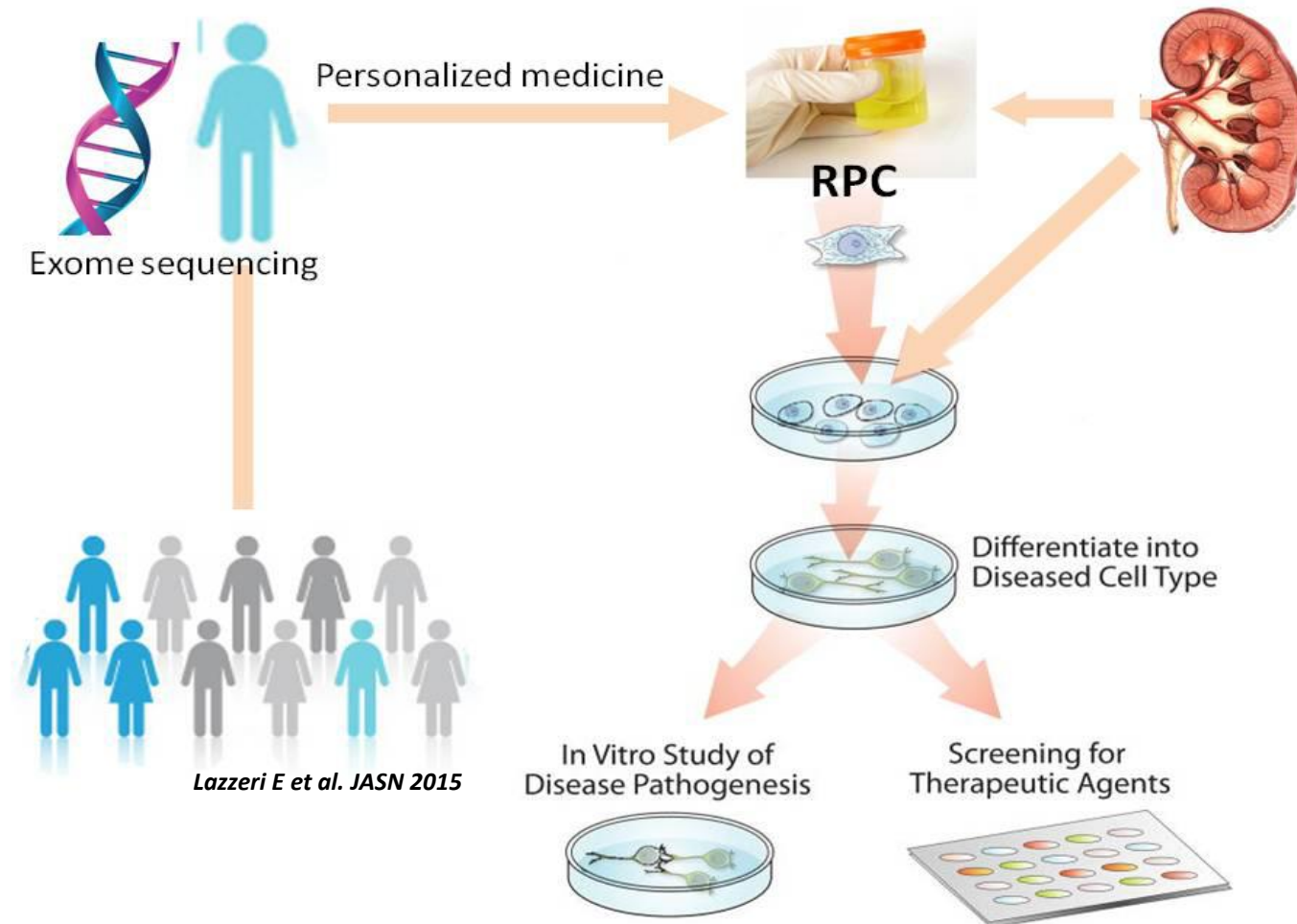
A personalized model of the disease



Lazzeri, E. & Romagnani, P. (2014) Differentiation of parietal epithelial cells into podocytes
Nat. Rev. Nephrol. doi:10.1038/nrneph.2014.218

Human Urine-Derived Renal Progenitors for Personalized Modeling of Genetic Kidney Disorders

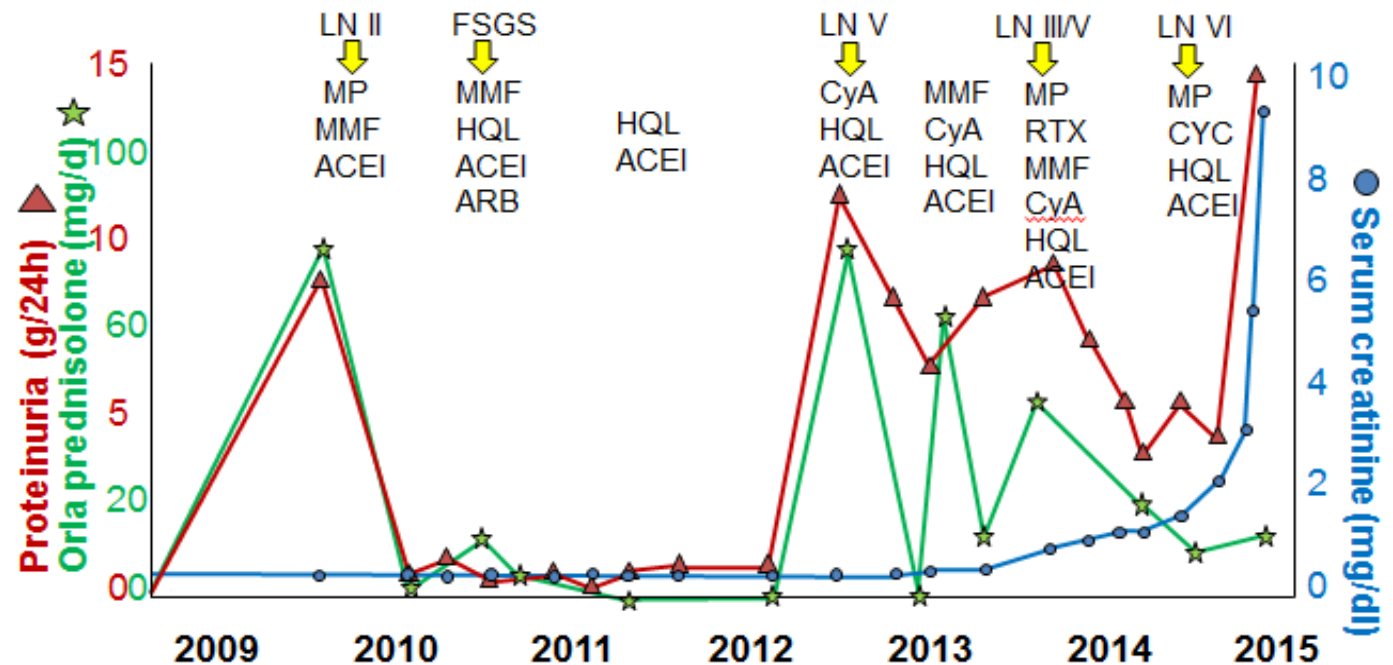
Elena Lazzeri,^{*} Elisa Ronconi,^{*†} Maria Lucia Angelotti,^{*} Anna Peired,^{*†}
Benedetta Mazzinghi,[‡] Francesca Becherucci,[§] Sara Conti,^{||} Giulia Sansavini,[§]
Alessandro Sisti,^{*} Fiammetta Ravaglia,[§] Duccio Lombardi,^{*} Aldesia Provenzano,[‡]
Anna Manonelles,[¶] Josep M. Cruzado,[¶] Sabrina Giglio,^{†‡} Rosa Maria Roberto,[§]
Marco Materassi,[§] Laura Lasagni,^{*} and Paola Romagnani^{*†§} *J Am Soc Nephrol* 26: 1961–1974, 2015.



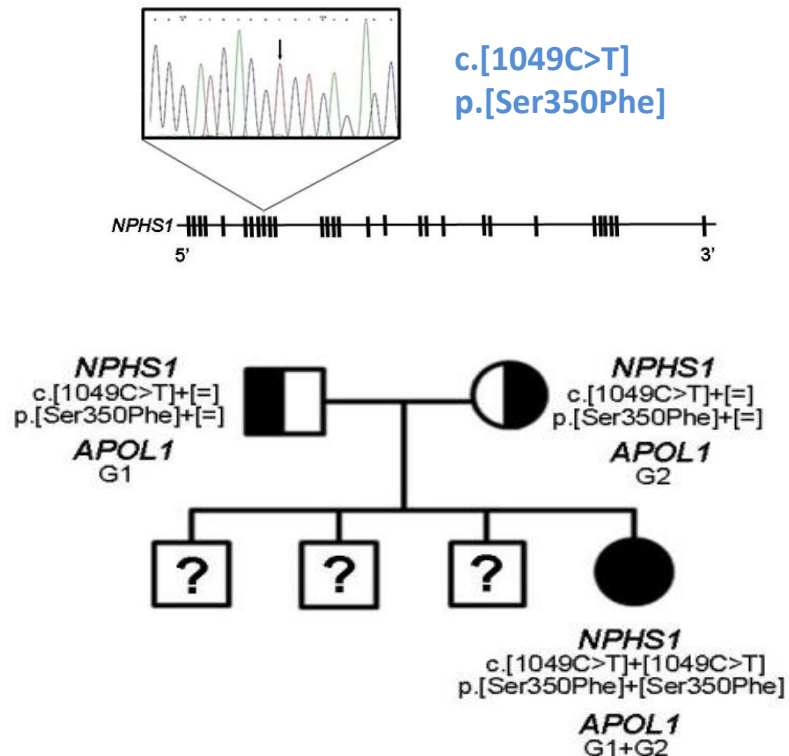
The Bench-to-Bedside Transition

Next generation sequencing and functional analysis of patient urine renal progenitor-derived podocytes to unravel the diagnosis underlying refractory lupus nephritis

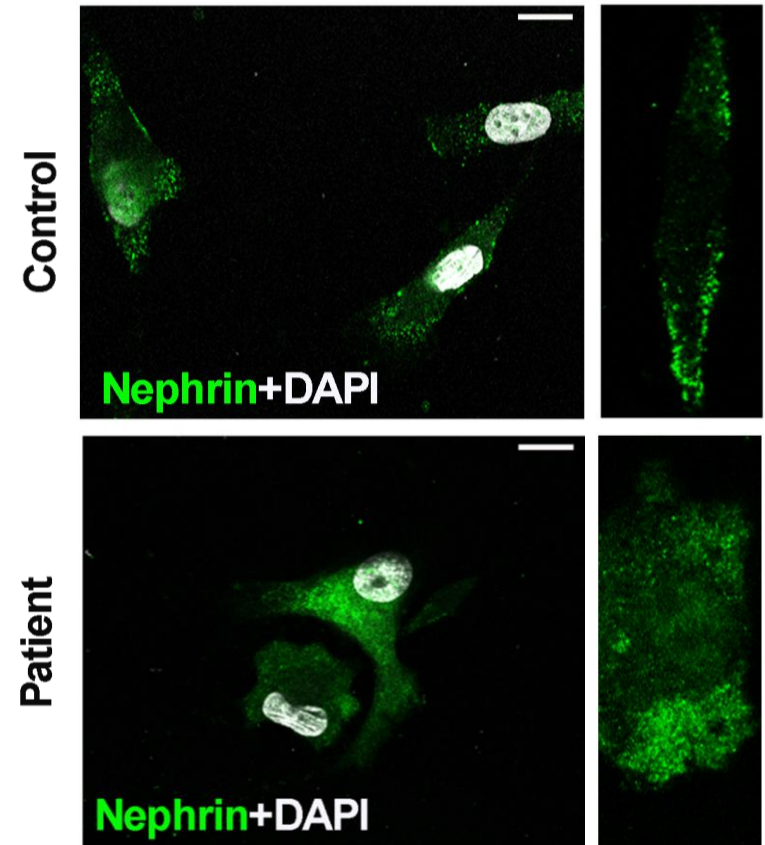
Paola Romagnani^{1,2,*}, Sabrina Giglio^{1,3,*}, Maria Lucia Angelotti⁴, Aldesia Provenzano³, Francesca Becherucci², Benedetta Mazzinghi², Susanna Müller⁵, Kerstin Amann⁶, Marc Weidenbusch⁷, Simone Romoli⁷, Elena Lazzeri⁴ and Hans-Joachim Anders⁷



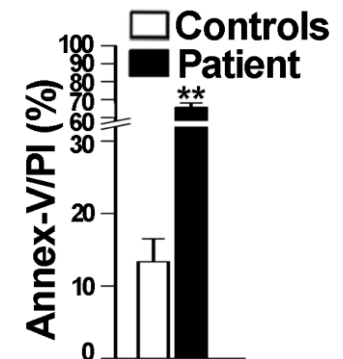
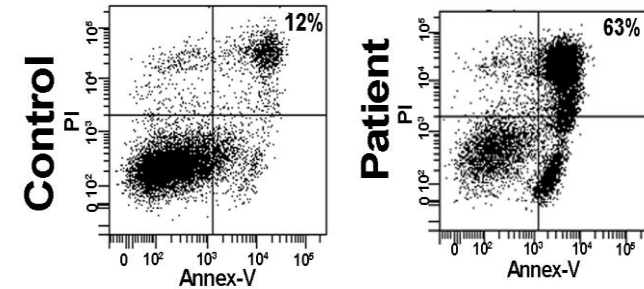
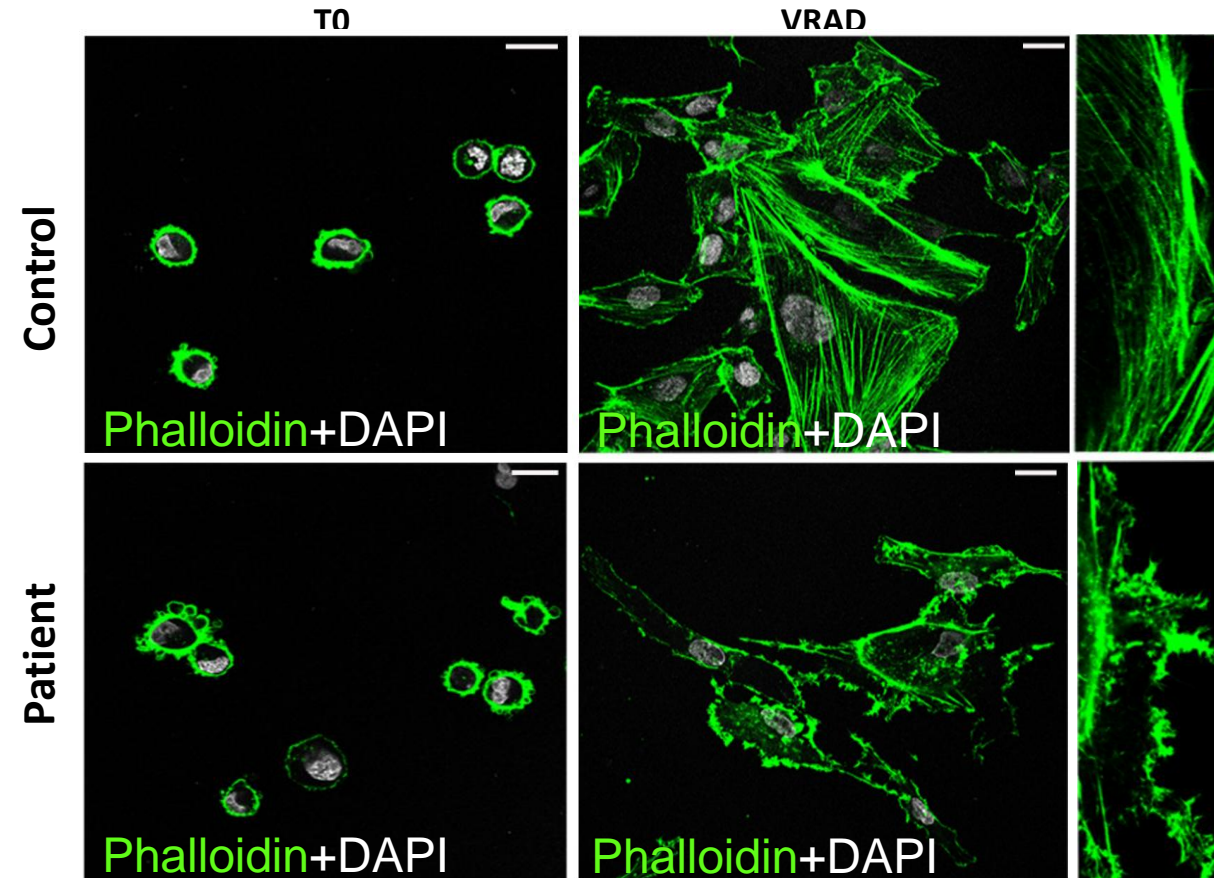
Resistance to immunosuppressive treatments associates with genetic alterations in podocyte structural genes



Romagnani P et al. *NDT*, 2016



Patient-specific RPC-derived podocytes show an aberrant cytoskeleton structure and increased death upon differentiation





2015

-Abbiamo iniziato a fare l'esoma a tutti i bambini affetti da SNSR e ad analizzare in ognuno 308 geni noti come causa di malattia renale cronica

-Nei bambini in cui individuiamo varianti sconosciute, i progenitori urinari possono essere utilizzati per dirimere dubbi diagnostici



ERC Starting Grant RESCARF 2008-2012

ERC Consolidator Grant RENOIR 2015-2020

Meyer Children's Hospital-University of Florence

Nephrology Unit

**Elena Lazzeri, Francesca Becherucci, Laura Lasagni,
Rosa Maria Roperto, Giulia Sansavini, Fiammetta
Ravaglia, Marco Materassi**

Genetic Unit

**Sabrina Giglio, Benedetta Mazzinghi, Aldesia
Provenzano**

