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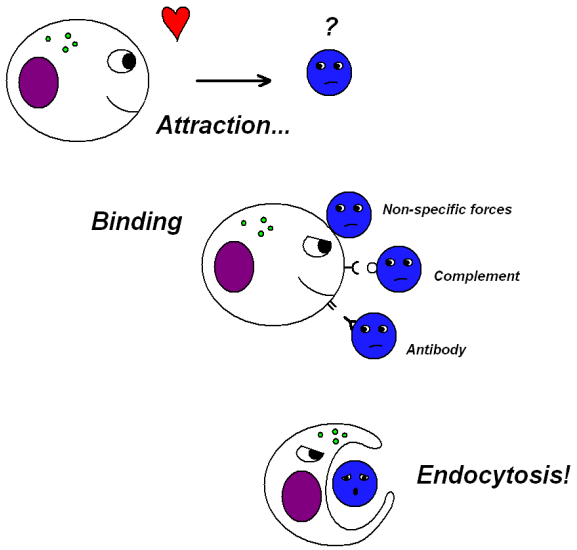
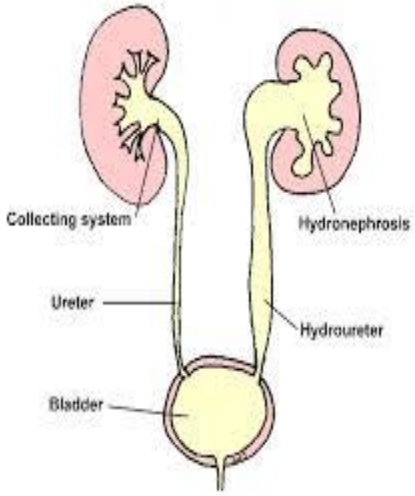
The main research interest:

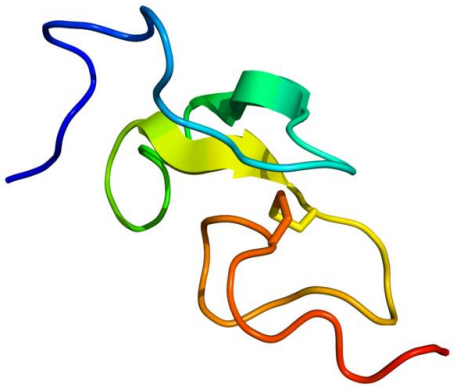
- The phagocytosis and distant migration of polydimethylsiloxane used for treatment of vesico-ureteral reflux in pediatric age

- The prevention and reduction of renal damage in children with congenital uropathy by studing cytokines

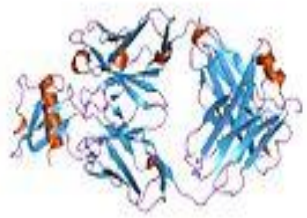




EGF



MCP-1



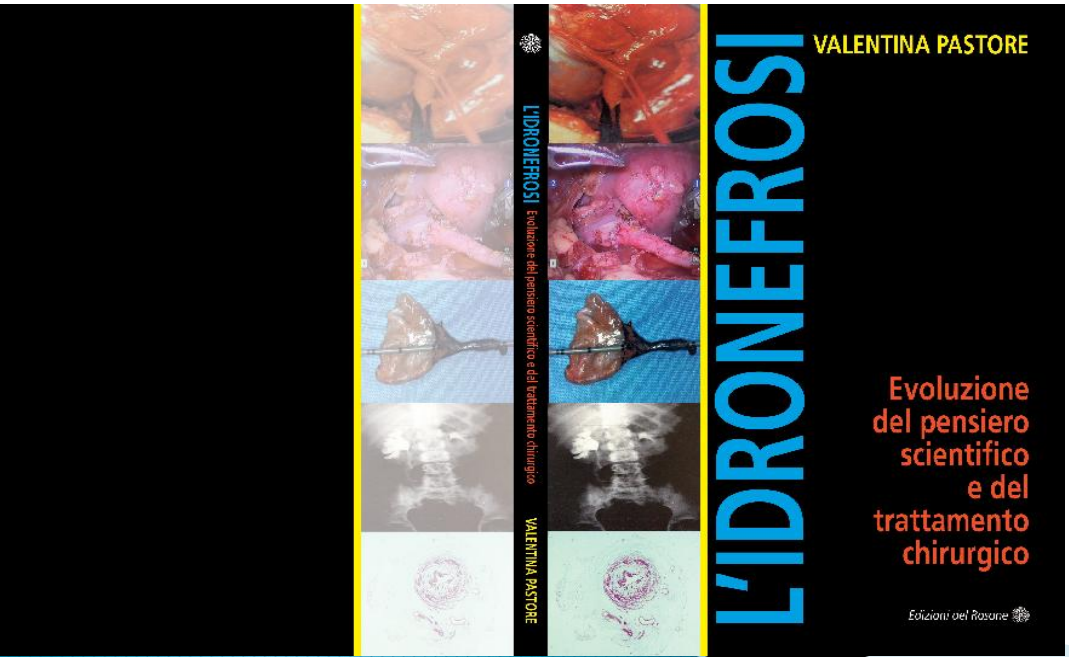
The research results and clinical outcomes have been presented at conferences

- 9th EUPSA Annual Meeting , Istanbul 18-21 June 2008
- Congresso Nazionale Congiunto 24-27 September 2008, Catania
- 3° Congresso Congiunto SICP,SIUP, SIVI 22-25September 2010, Torino
- 3rd World Congresso of Pediatric Surgery, 21-24 October 2010, New Delhi
- La ricerca clinica e sperimentale in chirurgia endoscopica e mini-invasiva pediatrica. 21 May 2011, Napoli
- 4° Congresso Congiunto SICP,SIUP, SIVI 21-24 September 2011, Padova
- Papsa Congress 2012. 18-21 March 2012, Cape Town

The research results and clinical outcomes have been published

- F Bartoli, R Penza, G Aceto, F Niglio, O D'Addato, **V Pastore**, V Campanella, S Magaldi, C Lasalandra,G Di Bitonto,L Gesualdo. Urinary egf, mcp-1 and ß2 microglobulin in children with ureteropelvic junction obstruction. J Pediatr Surg. 2011; 46 (3):530-6
- Bartoli F, Niglio F, **Pastore V**, Campanella V, Leggio S, Aceto G, Germano M, D'Addato O, Penza R. Polydimethylsiloxane (macroplastique) injection for vesicoureteral reflux in duplex ureter: a comparison with single renal systems. J Pediatr Urol 2011; 7 (5): 516-519
- **Pastore V**, Aceto G, Niglio F, Basile A, Cocomazzi R, Faticato MG, Lotito A, Bartoli F. Clinical characteristics and management of children with ureteropelvic junction obstruction and severe vesicoureteral reflux: preliminary results. Annals of Pediatric Surgery 2013; 9 (3): 114-116
- **Pastore V,** Aceto G, Niglio F, Basile A, CocomazziR, Faticato MG, Bartoli F. Laparoscopic assisted nephroureterectomy for shape urolithiasis and xantogranulomatous pyelonephritis. Case report and review of literature. African Journal of Pediatric Surgery 2013; 10: 285-288

All the results with a retrospective review of all the surgical techniques applied in children have been discussed in a book:



V. Pastore.
L'idronefrosi. Evoluzione del pensiero scientifico e del trattamento chirurgico.
Edizioni del Rosone, December 2013
ISBN 978-88-97220-99-2


RESEARCH

NEW RESEARCH PROJECT

Research on molecular pathways of renal damage and their modulation in experimental and clinical models of congenital uropathy by using nanocarriers

BACKGROUND/ STATE OF THE ART

1. In the last years, the interest of clinicians has focused on the potential role of plasmatic and urinary markers of renal function for early detection and monitoring of chronic kidney disease bacause pro-inflammatory cytokines or growth factors play a major role in activating apoptotic signalings which are the main factors to cause tubular atrophy and epithelial to mesenchymal transition [1,2]
2. The main factors triggering injury to the kidney are stretching and loss of integrity of tubular epithelium, followed by an inflammatory response mainly mediated by monocyte [3]

3. Reactive oxygen species play an important role in traslating inflammatory responce into cellular death, so that their monitoring is of detrimental importance to understand the responce to drugs [4]
4. Treatments with drugs often require high drug concentrations in the kidney and unfortunately such high concentrations are often associated with adverse effects. Furthermore, high renal drug concentrations may not translate into high concentrations in the target cells.
5. Kidney-targeted drug delivery is of great significance to overcome these problems and new anti-apoptotic therapies carried by nanocarriers have been proposed [5,6]

AIM 1

As first step of this new research, the role of oxidative stress and inflammatory process on the mitochondrial function, in animal models of obstructive and reflux nephropathy, will be assessed.

Genic expression which control :

- mitochondrial biogenesis
- apoptosis and macro-autophagia
- oxidative homeostasis

will be studied by using renal cellular homogenate.

At scheduled time urinary samples will be obtained to test Creatinine, MCP-1, EGF Beta-2 microglobulin.

AIM 2

Nanaocarriers will be prepared and drugs linked to them (inhibitors of apoptosis signal and anti-fibrotic drugs) will be administered to experimental animal mdels [7].

At scheduled time new urinary samples will be obtained to test Creatinine, MCP-1, EGF Beta-2 microglobulin.

AIM 3

After the approval of Ethic Commission, patients with grade 3 and 4 hydronephrosis and high grade vesico-ureteral reflux will be enrolled in the study to receive administration of intravesical compound embedded with specific anti-apoptotic and anti-fibrotic drugs. Urinary samples will be the only biological sample collected before treatment and at scheduled follow-up.

MILESTONE/ INNOVATION

To understand the impact of the mechanism of inflammatory injury on mitochondrial function and the ability to restore normal mitochondrial function by administration of drugs carried by nanocarriers.

Children seriously affected by urological conditions, in adult age, will be at risk for developing high blood pressure, cardiovascular diseases and renal tumor and insufficiency [8]

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2) Sanz AB et al. TWEAK and the progression of renal disease: clinical translation. Nephrol Dial Transplant 2014; 29 Suppl 1: i54-i62
3) Meng XM et al. Inflammatory processes in renal fibrosis. Nat Rev Nephrol 2014. doi: 10.1038/nrneph.2014.114
4) Salzano S et al. Linkage of inflammation and oxidative stress via release of glutathionylated peroxiredoxin-2, which acts as a danger signal. Proc Natl Acad Sci USA 2014 pii:201401712
5) Ucero AC et al. A polymeric nanomedicine diminishes inflammatory events in renal tubular cells. PloS One 2013; 8: e51992
6) Guhasarkar S et al.Intravesical drug delivery: challenges, current status, opportunities and novel strategies. J Control Release 2010; 148:147-159
7) Loyer P et al. Natural and synthetic poly(malic acid)-based derivates: a family of versatile biopolymers for the design of drug nanocarriers. J Drug Target 2014; 22: 556-575
8) Driver TH et al. Urinary kidney injury molecule 1 (KIM-1) and interleukin 18 (IL-18) as risk markers for heart failure in older adults: the health, aging, and body composition (ABC) study. Am J Kidney Dis 2014; 64:49-56