ImmunoTools *special* Award 2018

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The effect of urinary extracellular vesicles in kidney regeneration

Acute Renal Injury (AKI), characterized by an abrupt and sustained decline in glomerular filtration rate (GFR), is caused by an ischemic or nephrotoxic insult. The ability of the kidney to recover from AKI and regain normal function, determines the development of acute renal failure. During the last few years a considerable effort is being made in the development of novel therapies targeting this renal disease. Several studies base their research on the potential role of extracellular vesicles (EVs) in kidney damage restoration.

EVs are small vesicles, released by various cell types, that carry membrane and cytoplasmic constituents characteristic of their cells of origin facilitating intracellular communication. EVs can be found and isolated in several biological fluids such as saliva, urine, and serum. It has been suggested that EVs derived both from embryonic and adult stem cells can be used as a vehicle to shuttle proteins and genetic information between cells. *(Ratajczak et al. (2006)., Deregibus MC et al.(2007), Yuan A et al. (2009), Collino F et al.(2010)*

Our group has previously demonstrated that EVs derived from adult human mesenchymal stem cells (MSCs) contribute to kidney repair in glycerol-and ischemia-reperfusion-induced AKI *(Bruno S, Grange C, Collino F, Deregibus MC, Cantaluppi V, et al. (2012).*

Furthermore, we have also isolated $CD133^+$ cells from human renal tissue which have been identified as potential kidney stem and progenitor cells (KSPCs). These cells exhibit both embryonic renal (Pax-2) and mesenchymal stem cell markers like CD29, CD73 and CD90 *(Bussolati et al 2005, Bussolati et al 2009, Bussolati et al 2012, Moggio et al 2012).*

In my project, I am evaluating whether EVs derived from adult $CD133^+$ progenitors and urine, a source of EVs secreted by $CD133^+$ kidney cells, can be used as a potential therapeutic renoprotective intervention to restore AKI damage. It has been demonstrated that EVs circulating along the nephron, while mediating intranephron

communication, can be found and isolated in urine (uEVs) *(Ranghino A. 2015).* In addition, *in vitro* experiments have shown that EVs derived from kidney cells facilitate the transfer of active molecules *(Ranghino A. 2015).*

For my project I am first characterizing different urine-derived EV populations in order to identify their cells of origin. After a complete characterization, I aim to administer these uEVs in an *in vitro* model of AKI involving renal tubular cells to evaluate protein cargo transfer and possible renoprotective-regenerative effects. In addition, following complete characterization and *in vitro* experiments, the next step would be to evaluate the effects of uEVs in AKI mice models *in vivo* already established in our Lab.

The requested antibodies and factors will be of high importance for my project as they will allow the characterization of renal derived EVs (isolated by renal progenitor cells and urine), as well as the evaluation of their cargo transfer to recipient cells both in *vitro* and *in vivo*. The biological activity of uEVs and renal progenitor cell-derived EVs on kidney cell damage will be assessed *in vitro* and *in vivo* through the evaluation of apoptosis, cell proliferation-regeneration, as well as inflammation. Therefore, it would be advantageous to include exosomal markers for proper extracellular vesicle characterization, as well as cytokine EIISA kits for the assessment of inflammation.

ImmunoTools *special* Award for **Elli Papadimitriou** includes 24 reagents

PE - conjugated anti-human CD63, CD147

APC - conjugated anti-human CD105

recombinant human cytokines: rh CTGF, rh FGF-23, rh IFN-gamma, rh VEGFR2

human ELISA set (for one 96 plate): human IL-6, human IL10, human TNF-a

recombinant mouse cytokines: rm TNF-a

mouse ELISA set (for one 96 plate): mouse TNF-a

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