

Milos MIHAJLOVIC

PhD student / ESR 5

PhD on

Bioartificial kidney
Preclinical safety evaluation

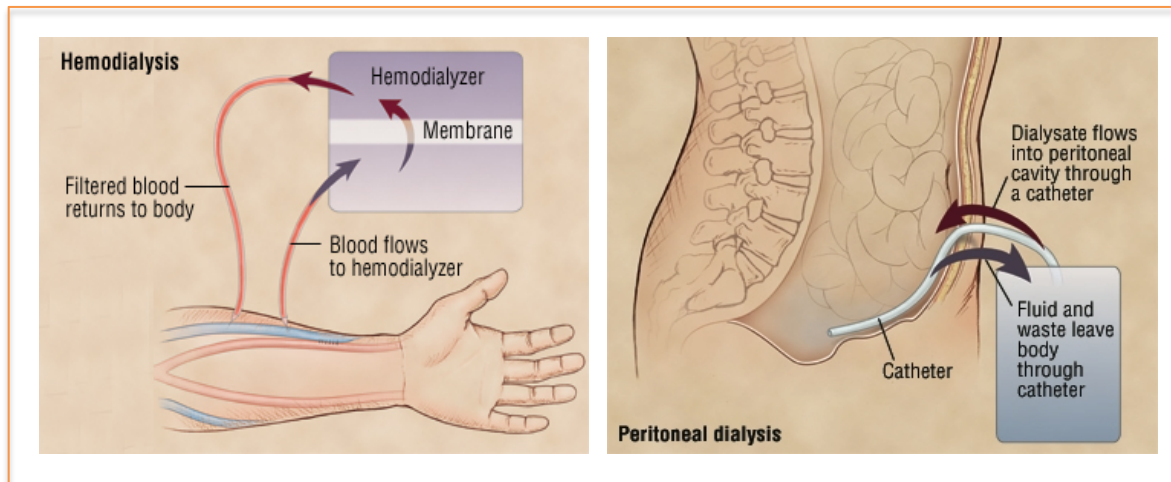
Aim & Things done
October 2014

PhD start date: December 2013

RUNMC, The Netherlands

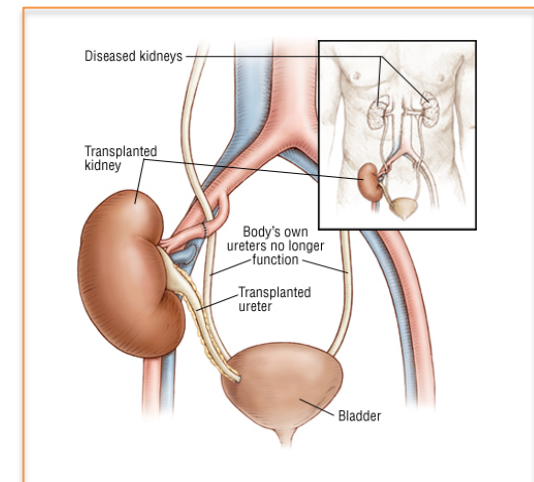
End Stage Renal Disease (ESRD) – current treatments

Dialysis



- high cost
- inefficient in removing waste molecules and excess body fluids, potassium and phosphate

Kidney transplantation

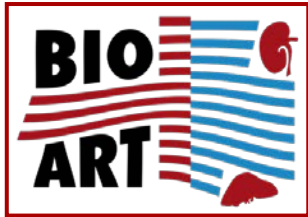
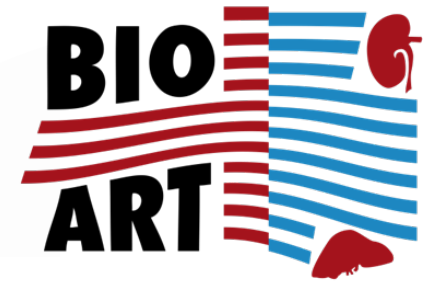


- limited availability of donated kidneys
- side effects related to immunosuppressive therapy



Poor life quality and high mortality (15-20%)

ESR-5: Bioartificial kidney – Preclinical safety evaluation

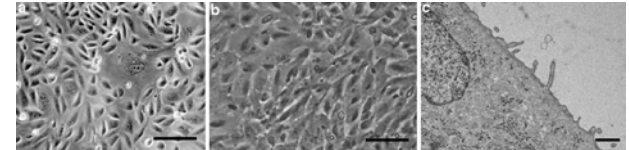


(WP2 - AIM) Develop prototype **bioartificial kidney device** that utilizes human renal epithelial cells for more efficient removal of uremic toxins in order to improve the treatment of ESRD



- Use of immortalized human renal epithelial cells that grow in a monolayer, and possess all the transport characteristics required for the removal of protein bound toxins
- Development of bioactive membranes to support the renal epithelial cells

conditionally immortalized proximal tubule epithelial cells - *ciPTEC*



M.J. Wilmer et al., Cell Tissue Res - 2010



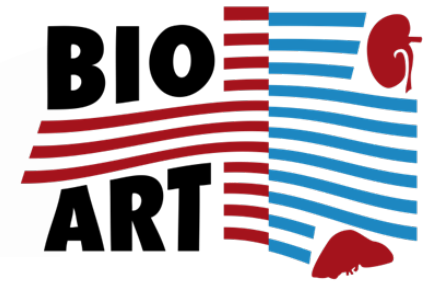
(ESR5) Bioartificial kidney – Preclinical safety evaluation

Evaluate the safety aspects of the bioartificial kidney:

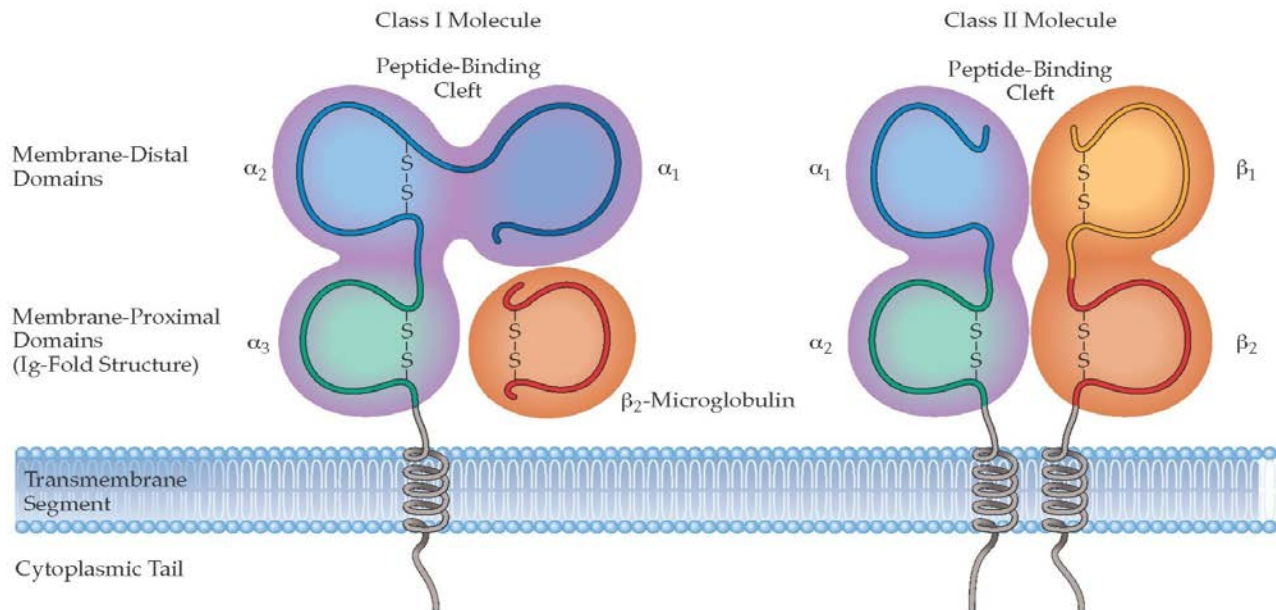
- Immune activation (allogeneic response) → Major Histocompatibility Complex (MHC) molecules
- Biocompatibility
- Transmission of oncogenes and/or pathogenic substances



Allogeneic response



Major Histocompatibility Complex (MHC)
Human Leukocyte Antigen (HLA) - nomenclature human



MHC class I

- found on nearly every nucleated cell of the body
- process and display cytosolic proteins
- activation of cytotoxic T cells

MHC class II

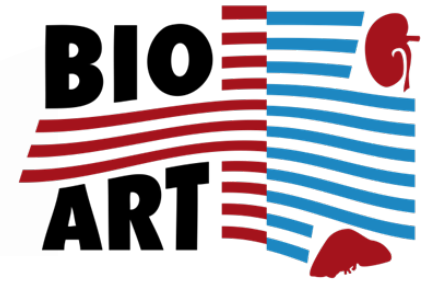
- found only on antigen-presenting cells and B cell lymphocytes
- process and display extracellular proteins
- activation of helper T cells

<http://what-when-how.com/acp-medicine/adaptive-immunity-histocompatibility-antigens-and-immune-response-genes-part-1/>

MHC molecules are highly polymorphic, and therefore can act as alloantigens and elicit both cell-mediated and humoral immune responses during transplantation procedures.



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