

New Opportunities Through Innovations

Jacques Pirenne, Transplant Surgeon, Leuven

Organ Shortage

Xenotransplants?

Artificial Organs?

Maximize Deceased Donor Pool

New Preservation Techniques

Maximize Living Donor Pool

*Journalist Workshop
Organ Donation & Transplantation
7 /10/ 2013*



Dependence upon Anti-Rejection Drugs

Chronic Graft Loss: Mechanisms

Toxicity: Minimize & Avoid Anti-Rejection Drugs

New Transplants

Regeneration & Organ Bioengineering : “Holey Grail”

Xenotransplants?



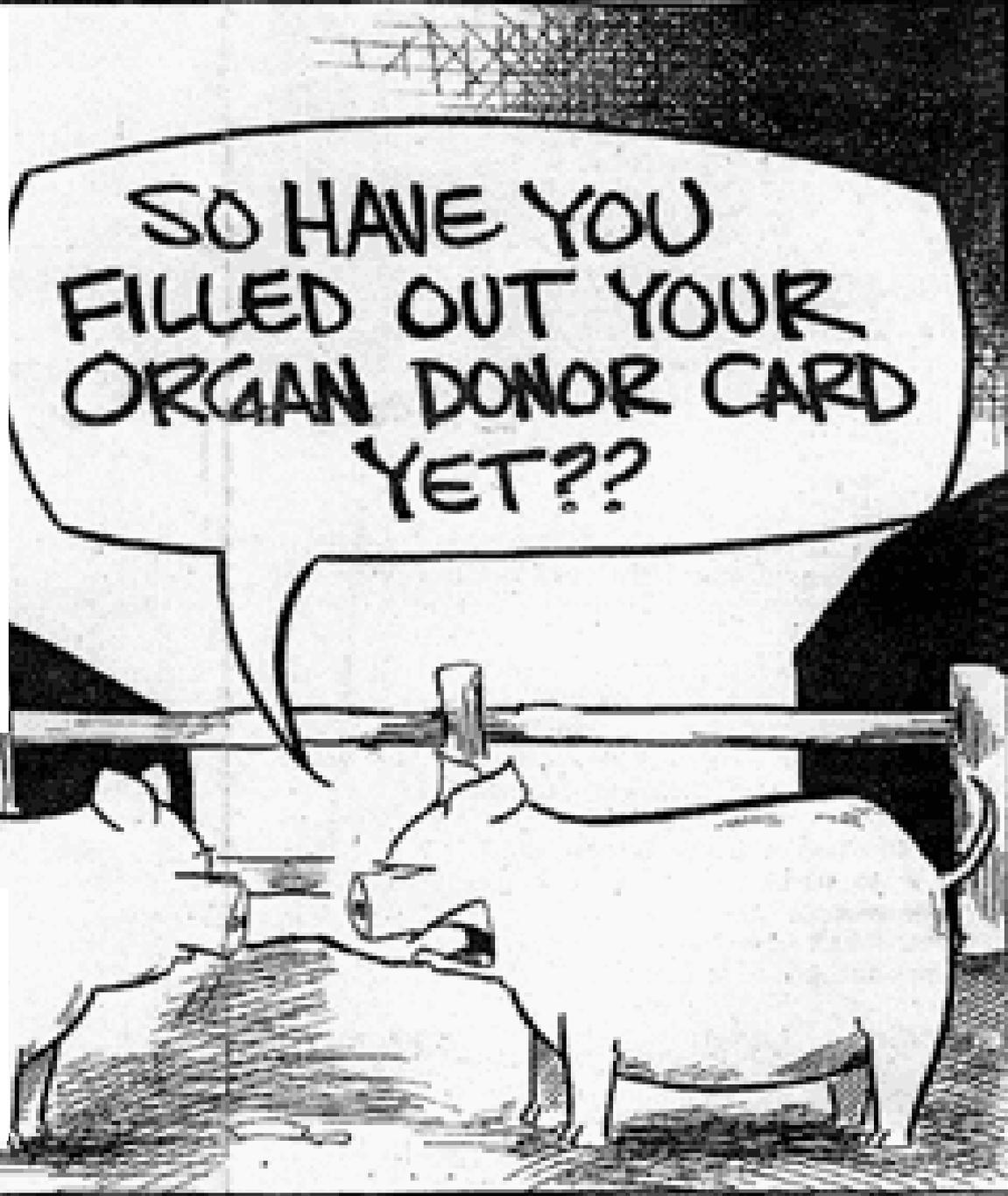
Chimps can benice guys too

- **Rejection**



Genetically modified pigs

- **Infection/Xoonosis?**
- **Physiological limits**



Xeno **cells** Transplant
Encapsulated islets
Neuronal cells

Artificial Organs?

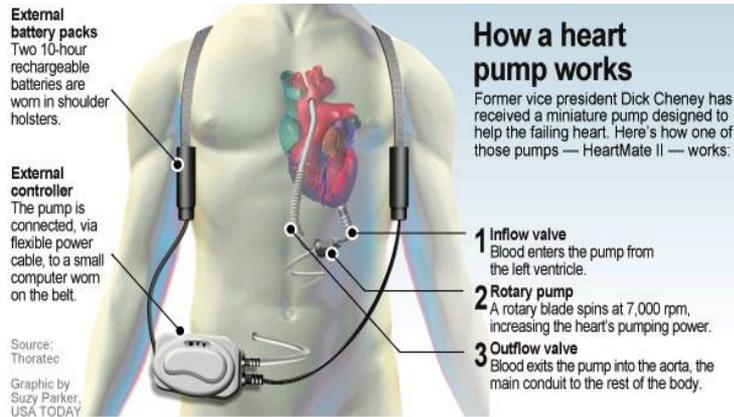
Kidney Dialysis



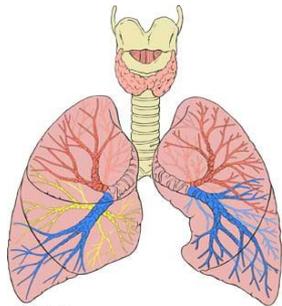
Ventricular Assistance Device



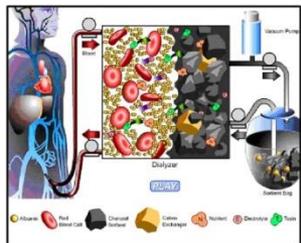
Fully Implantable Device



Lung: Extracorporeal Membrane Oxygenation

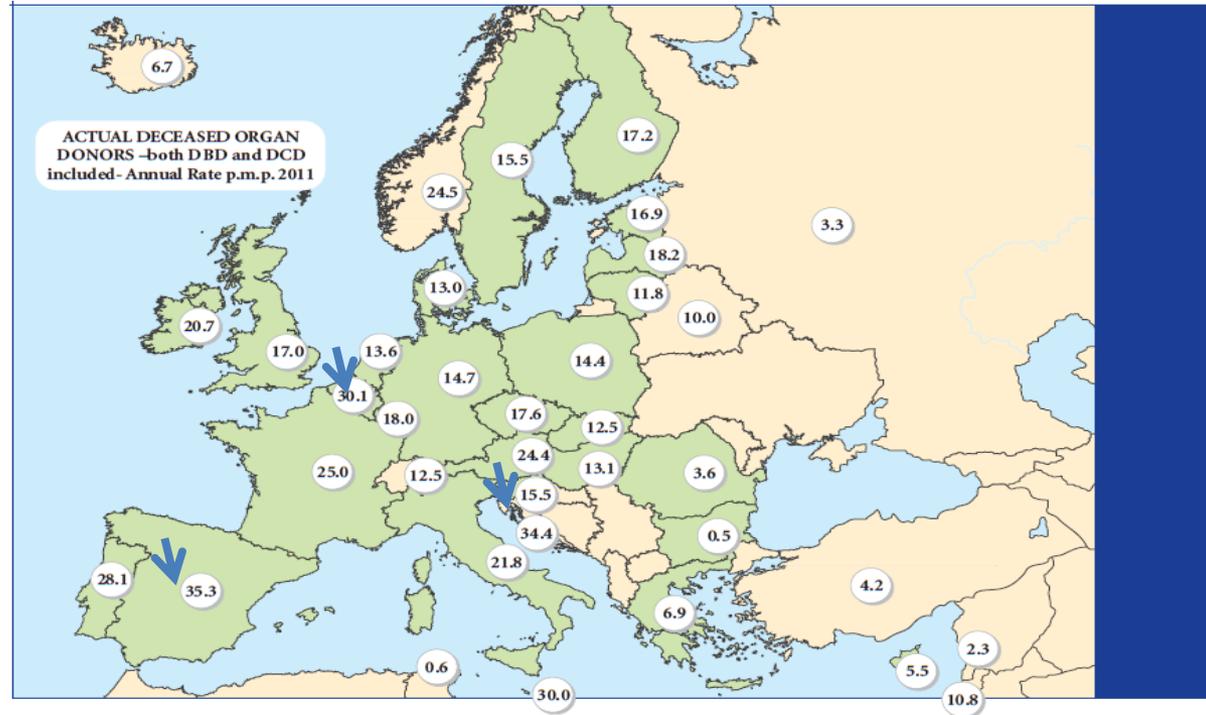


Liver "Dialysis"



Maximizing Deceased Donor Pool

Legislation



Detection

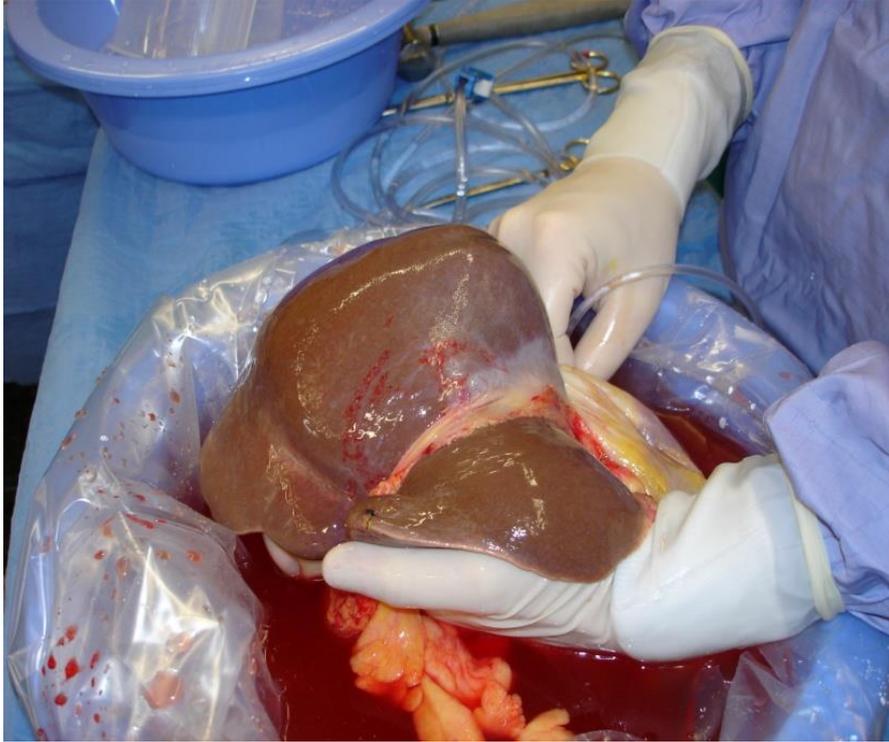
Training (para) medical staff

Optimize resources

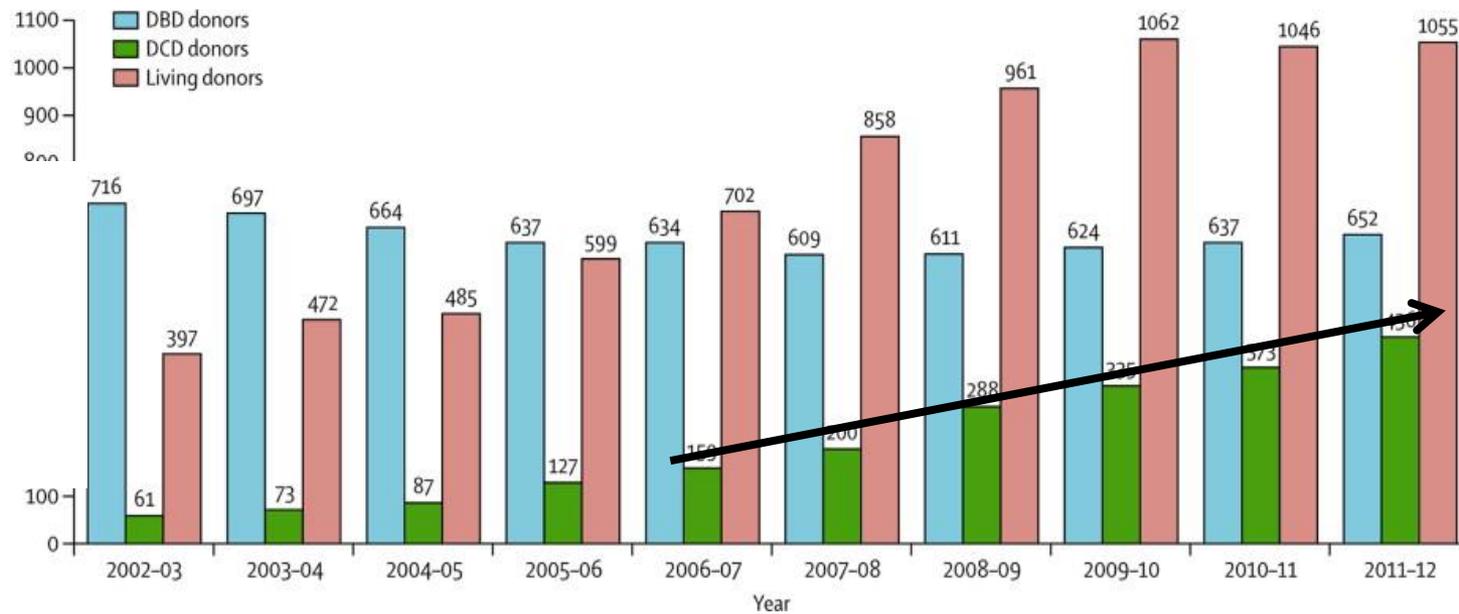


Extension of Donor criteria

82 yo donor liver

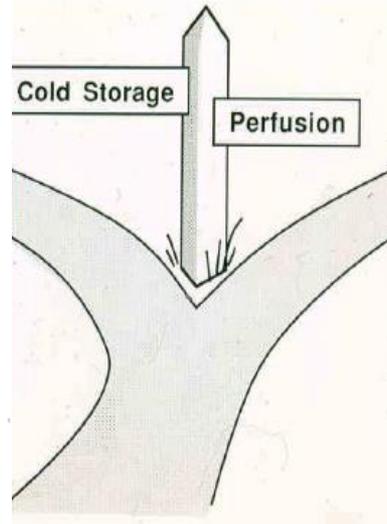


Donation After Circulatory Death (DCD) After euthanasia



New Preservation Techniques

Simple cold storage



Cold perfusion



The NEW ENGLAND
JOURNAL *of* MEDICINE

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Machine Perfusion or Cold Storage
in Deceased-Donor Kidney Transplantation

Cyril Moers, M.D., Jacqueline M. Smits, M.D., Ph.D., Mark-Hugo J. Maathuis, M.D., Ph.D., Jürgen Treckmann, M.D., Frank van Gelder, Bogdan P. Napieralski, Margitta van Kasterop-Kutz, Jaap J. Homan van der Heide, M.D., Ph.D., Jean-Paul Squifflet, M.D., Ph.D., Ernest van Heurn, M.D., Ph.D., Günter R. Kirste, M.D., Ph.D., Axel Rahmel, M.D., Ph.D., Henri G.D. Leuvenink, Ph.D., Andreas Paul, M.D., Ph.D., Jacques Pirenne, M.D., Ph.D.,

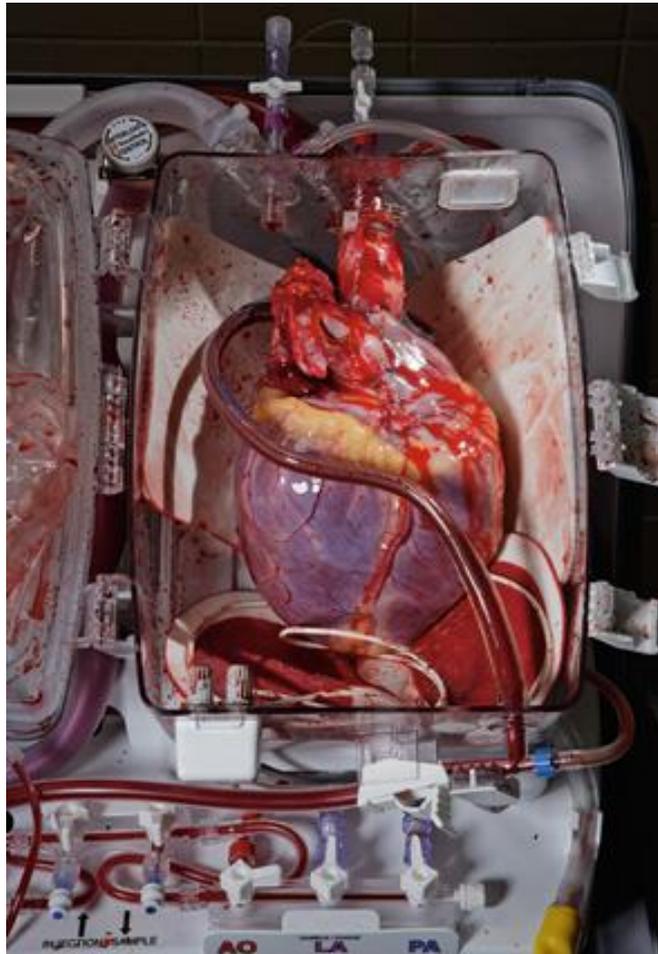


Better Function
Better Survival
Viability assessment

Warm Perfusion

Heart Proceed Trial

Mc Curry JHLT 2008



Evaluation of viability

Repair

Modulation*

against rejection, inflammation, infection

Better function posttransplant

Longer Preservation

**Via Drugs, trophic factors, viral vectors, siMRNA*



COPE

Consortium on organ preservation in Europe

- Technology for organ reconditioning and preservation
- Kidney + Liver
- Coordinator: Rutger Ploeg, Univ Oxford
- ESOT link
- EU contribution: €6 million
- Four clinical trials
- www.cope-eu.org





**First Successful
Kidney Tx 1953**

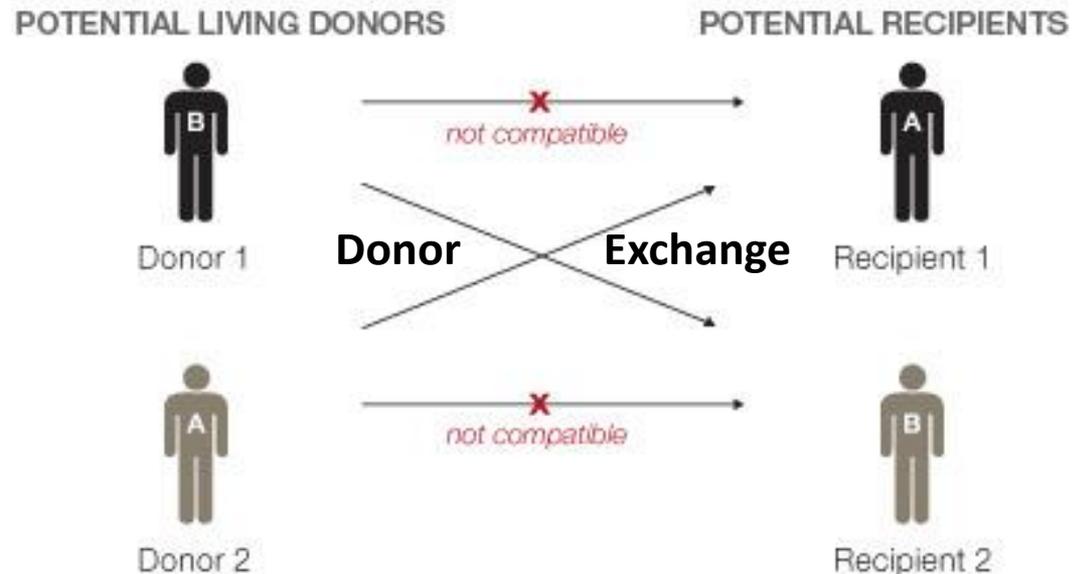
**Altruistic donors:
Genuine &
anonymous gift**

Maximizing Living Donor pool

**USA, Scandinavia, Holland: ~40-50%
Belgium, France: ~5-10%**

Information without coercion

ABO incompatible Tx



Altruistic Donors

- *Give*
- *Anonymously*
- *To unknown recipient*
- *With no counterpart*

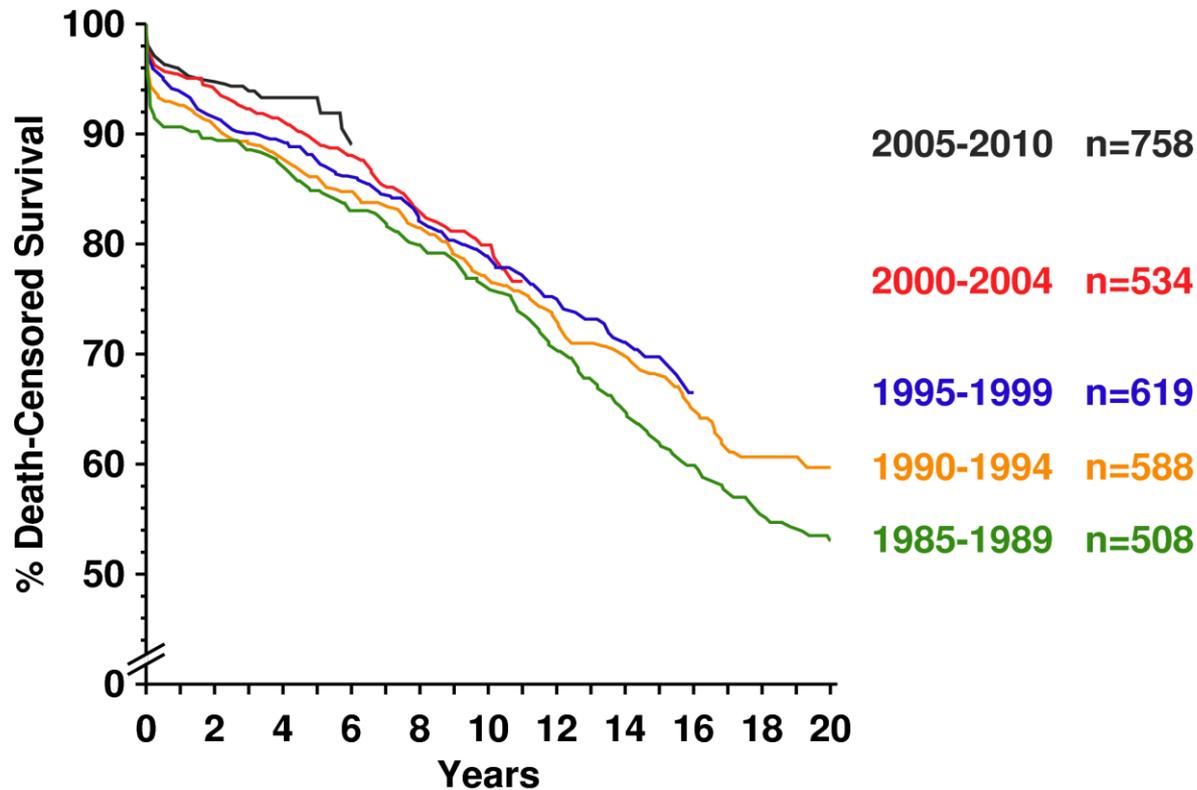
Parabole of the Good Samaritan
Stained glass window
St Eutrope, Clermont-Ferrand, France



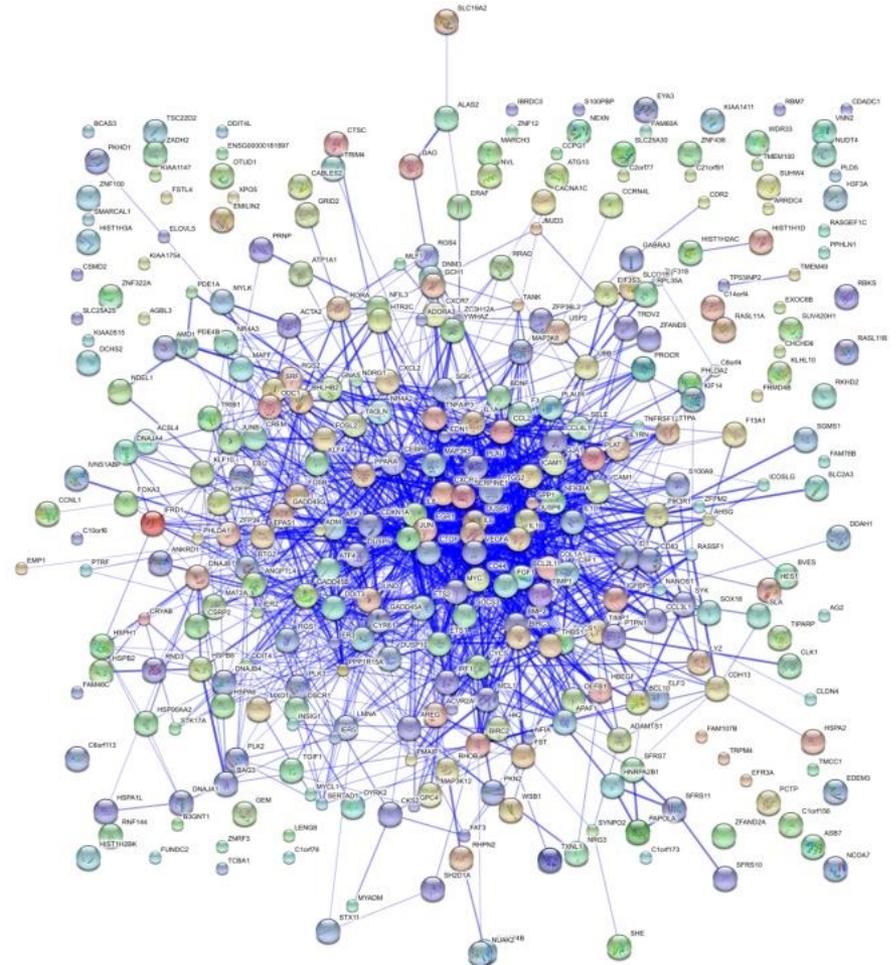
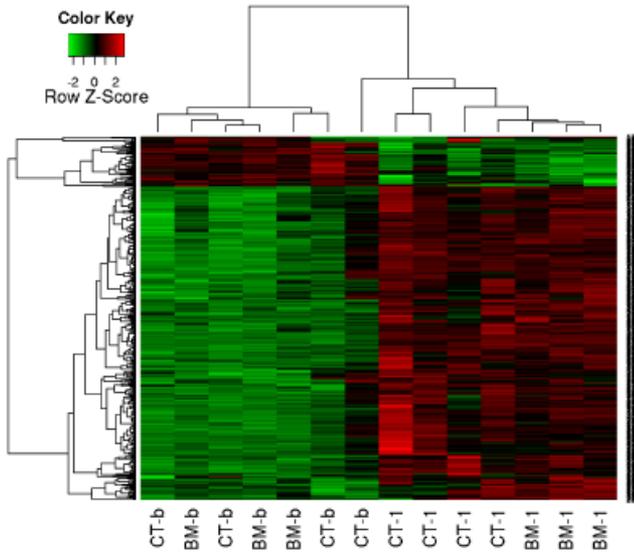
Chronic Graft Loss



KIDNEY TRANSPLANTATION: OUTCOME PER ERA



Transcriptome \longrightarrow **Bioinformatics**
Genes actively expressed \longrightarrow *Molecular Pathways Involved*



J van Liver Tx 2011

Naesens Nat Rev Nephrol 2010, Grigoryev JASN 2008, Akalin ISN 2010, Kotsch Tx 2010, Godwin PNAS 2010, Korbely Tx Int 2010



Biomargin



Biomarkers of renal graft injuries in kidney allograft recipients

- Coordinator: Pierre Marquet, INSERM, Limoges
- EU contribution: €6 million
- www.biomargin.eu

Minimizing Anti-Rejection Drugs



Why?

- Infection & Cancer
- Toxicity
- Costs
- Compliance
- Quality of Life

Minimization of anti-rejection drugs currently based on “trial and error”

BIO-DrIM

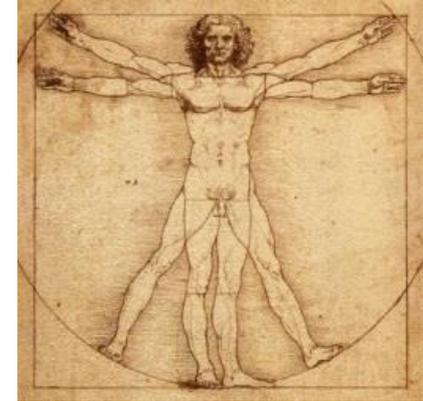


BIO-DrIM

Personalised minimisation of immunosuppression after solid organ transplantation by biomarker-driven stratification of patients to improve long-term outcome and health-economic data of transplantation

- Kidney + Liver
- Coordinator: Petra Reinke, Charité, Berlin
- EU contribution: €6 million
- Follow-on from FP5 (Indices of tolerance) and (FP6) Riset projects

Avoiding Anti-Rejection Drugs “Tolerance”



Peter Medawar

How?

Co-Tx of donor
immune cells

Problems?

Toxicity of preconditioning regimens
Predictors (signature) of tolerance
Recipient selection



The One Study

A unified approach to evaluating cellular immunotherapy in solid organ transplantation

- Cell product technology (Treg, Tr1, Mreg, DC)
- One clinical trial - kidney
- Coordinator: Ed Geissler, Univ Regensburg
- EU contribution: €10.8 million
- www.onestudy.org

Multi-Organ Transplants



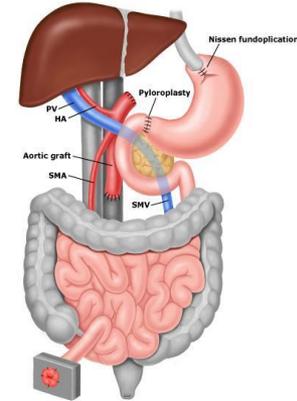
Liver + Kidney



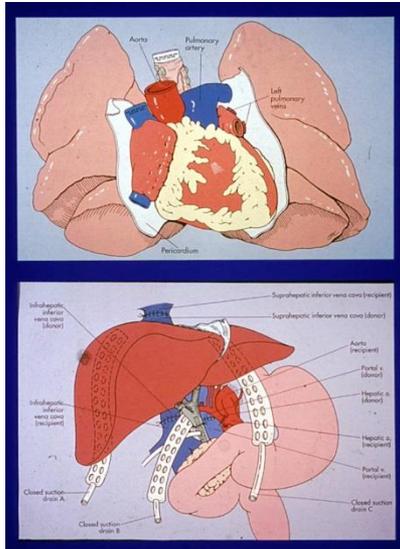
Liver + Pancreas



Liver + Bowel



Multivisceral



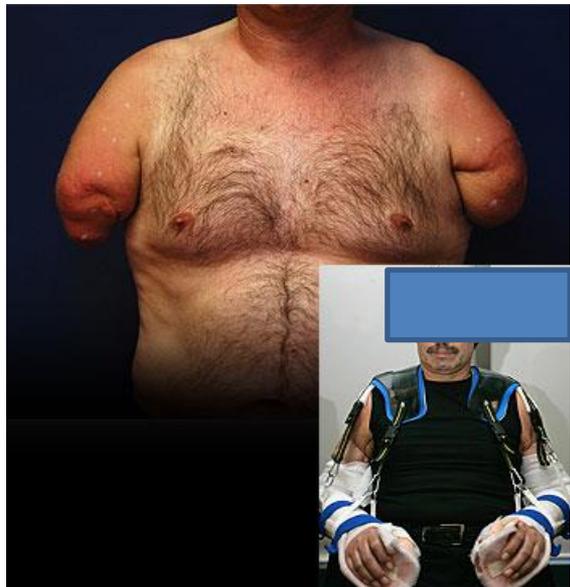
Liver + Heart

Liver + Lung

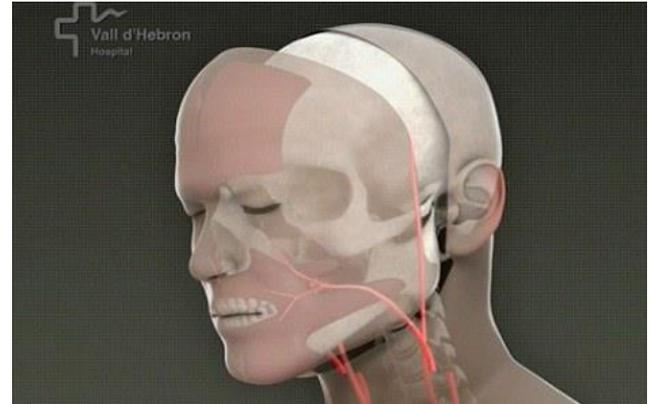
Liver + Heart + Lung

Composite Transplants

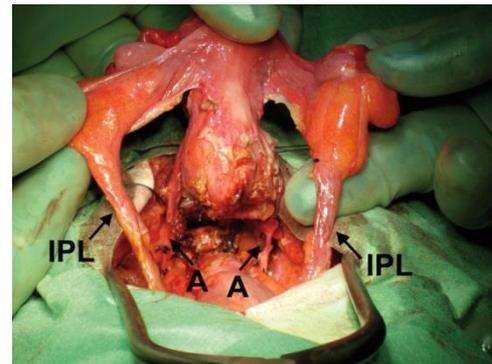
Limbs



Face

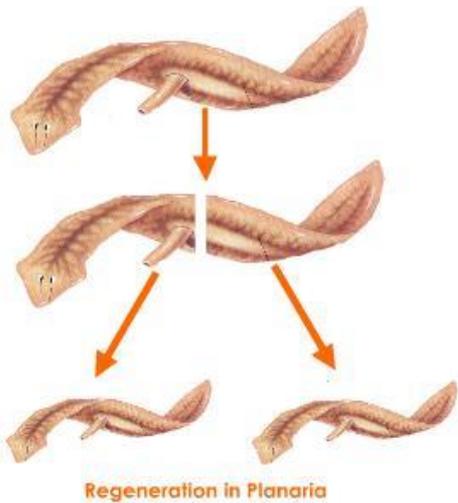


Uterus



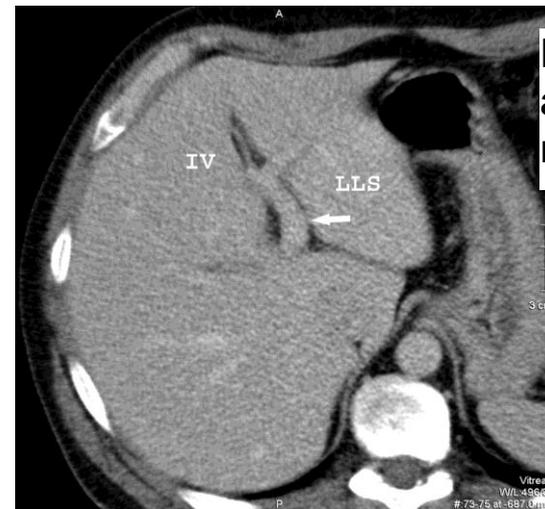
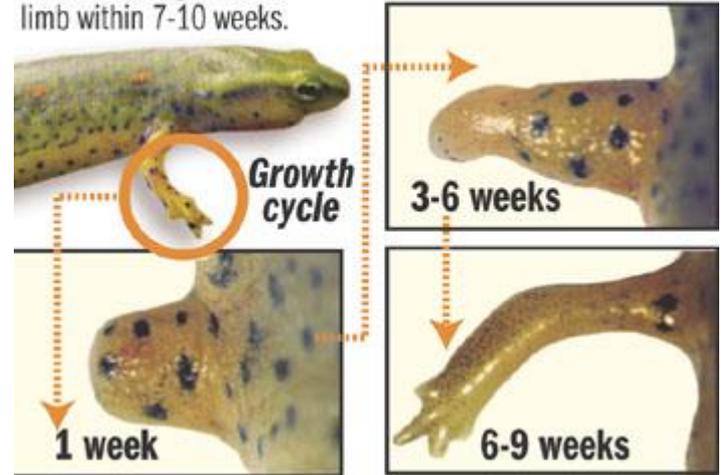
Regeneration

Each piece of a planaria regenerates in a complete organism



Regenerating a limb

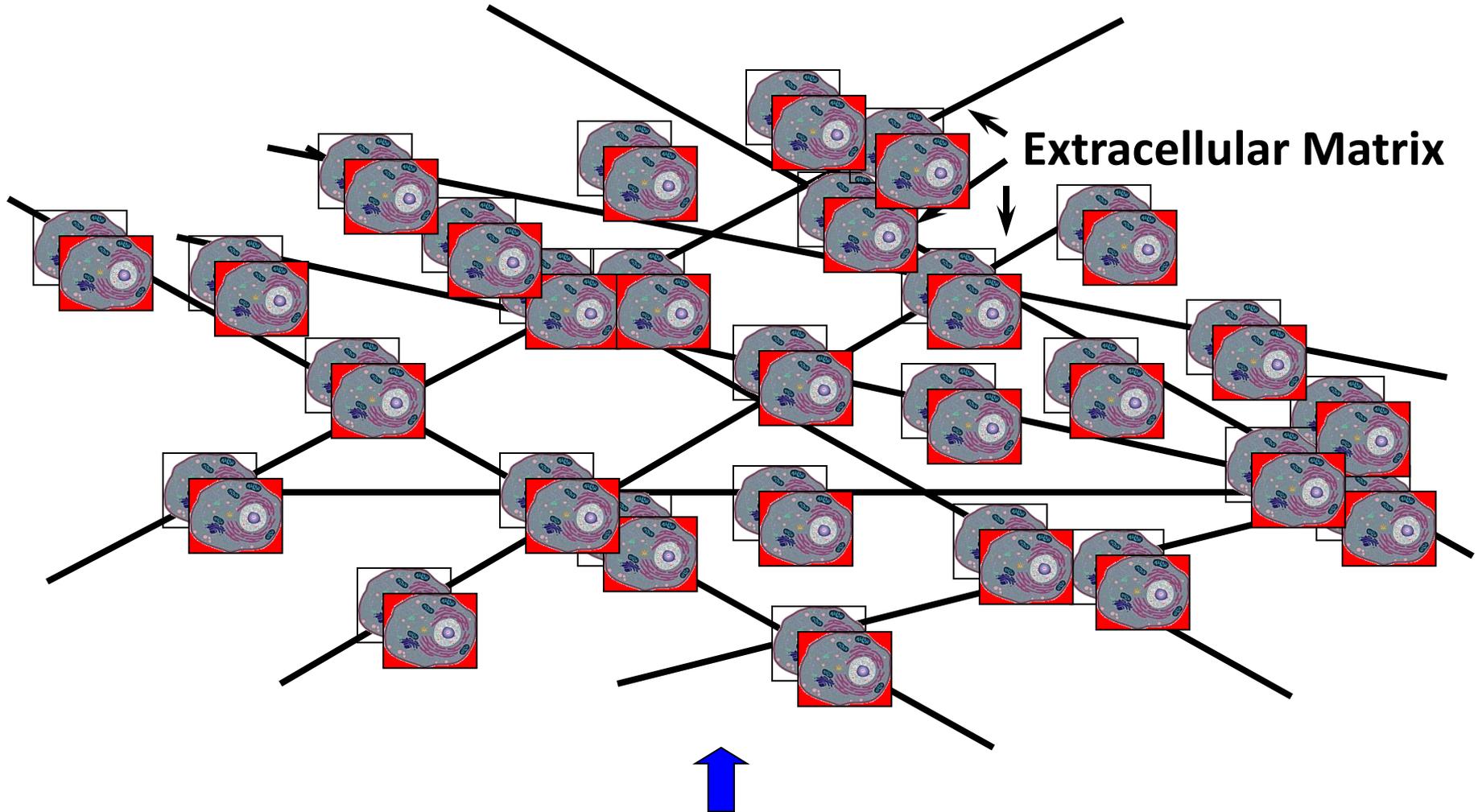
A newt can regenerate an entire limb within 7-10 weeks.



Liver regeneration after right lobe donation

Organ Bioengineering

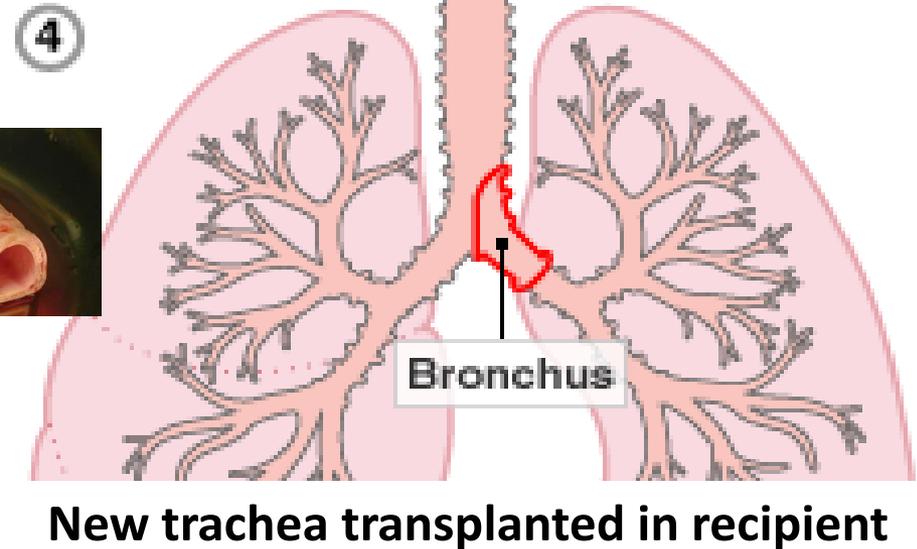
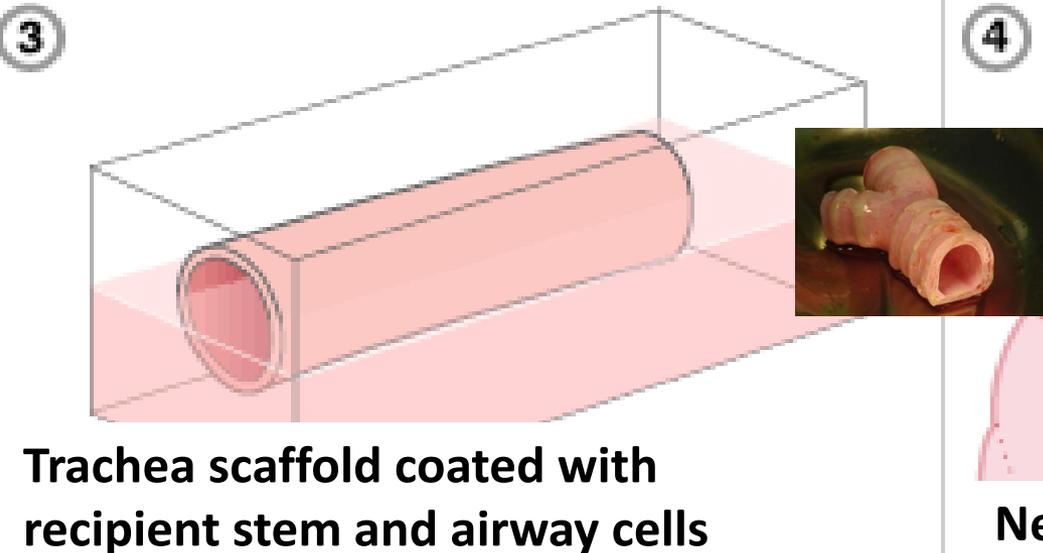
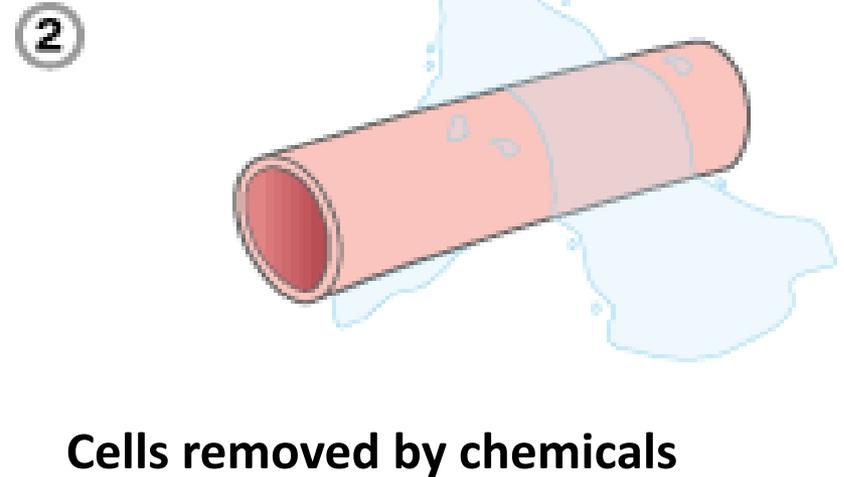
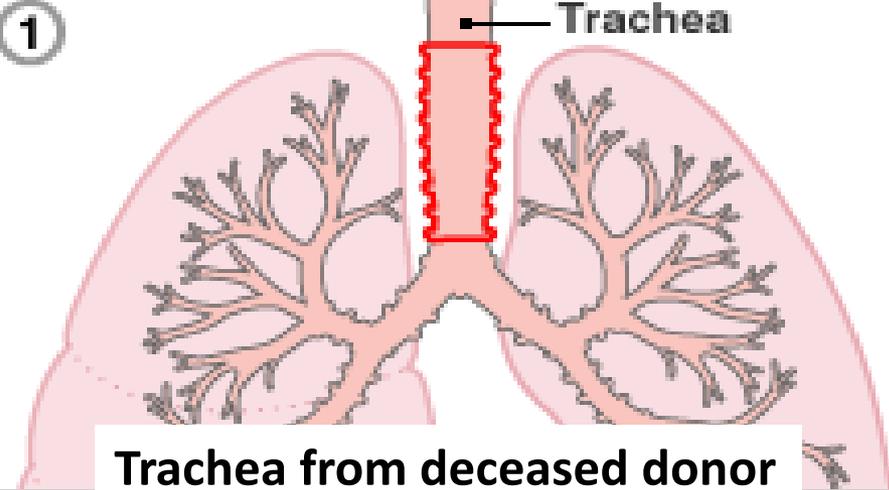
Organ = Matrix + Cells



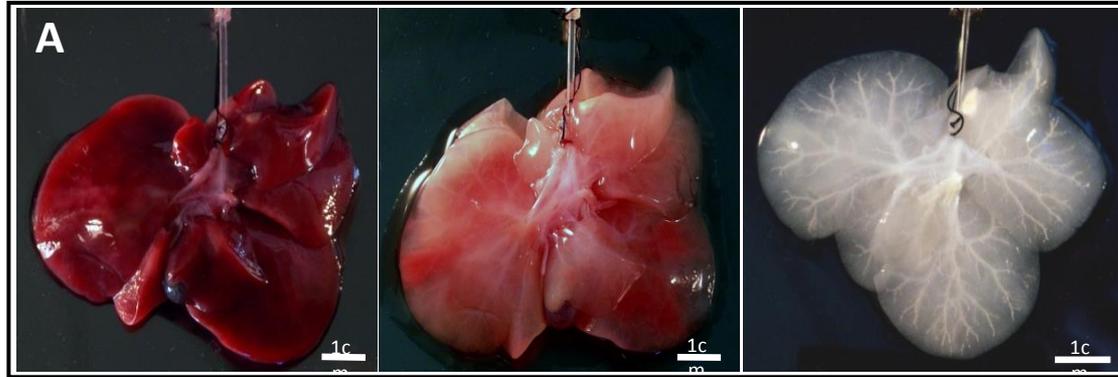
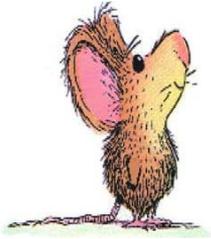
Triton X-100 + NH₄OH

Orlando G Organ bioengineering regeneration : new holy grail of transplantation ANN SURG, 2013

Construction of tubular organ



Construction of solid vascularized organ



Decellularization



Scaffold

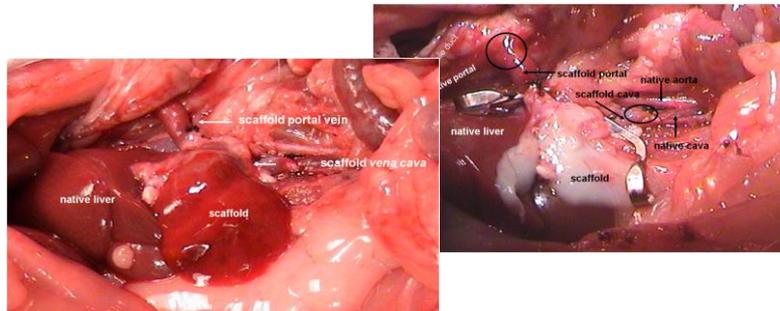


Transplantation

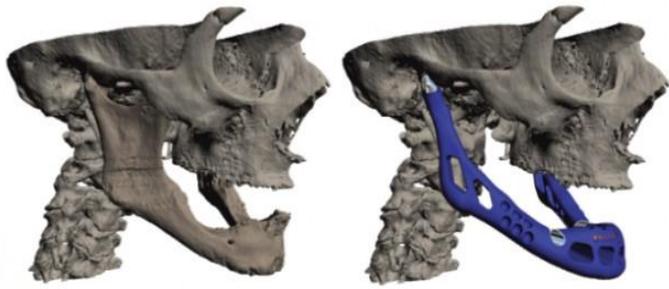


Recellularization

Liver Progenitor & Endothelial cells



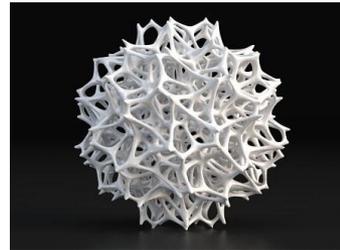
3D Printing



Simple Scaffold



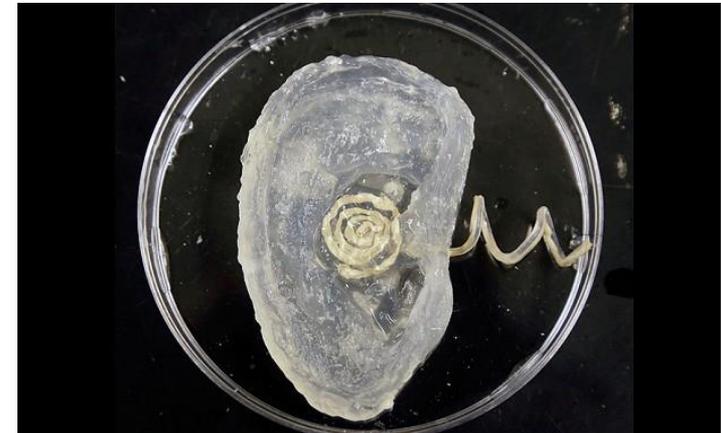
Complex Scaffold



Scaffold + cellular “printing”

Scaffold + cellular “printing” +
electronic

3D printed bionic ear



Conclusions

- **Solid organ Xenotransplants faced with biological obstacles? Cellular xeno Tx more likely to succeed**
- **Artificial organs bridge to transplant**
- **Maximize deceased donor pool: Legislation, detection, extension of criteria & public awareness**
- **Preservation: From “Ice box” to warm perfusion**
- **More information on living donation & ABO incompatible Tx**
- **Multi-organ & composite transplants increasingly performed**
- **Chronic graft loss: predictors, mechanisms and prevention**
- **Patient tailored minimization of anti-rejection drugs**
- **Successful reproducible induction of tolerance still to be achieved**
- **Organ bioengineering & regeneration may allow to construct new tissues/organs (eliminating waiting list) with own recipient cells (eliminating rejection)**



Recipients and donor families on the top of Mont-Blanc

9 september 2013