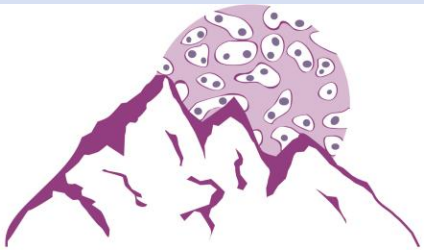
Welcome and opening remarks. History and future of the Banff Classification. Where the present lesion scoring criteria came from, and the continued need for ease of use and time efficiency. – Kim Solez, M.D.



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FOR ALLOGRAFT PATHOLOGY

Faculty / Presenter Disclosure

- Faculty: Kim Solez, M.D.
- Relationships with commercial interests:
  - None

The accreditation process was challenging. We almost gave up! But we succeeded with the help of student Patricia Bacus.

There is an analogy between challenges of accreditation and challenges of tissue engineering pathology and incorporating the human cell atlas project. We will succeed there as well!

- Please complete evaluation form!

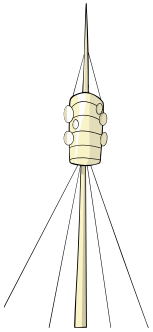
BANFF FOUNDATION
FOR ALLOGRAFT PATHOLOGY

THE CATALAN
TRANSPLANTATION
SOCIETY

SOCIETAT
CATALANA DE
TRASPLANTAMENT

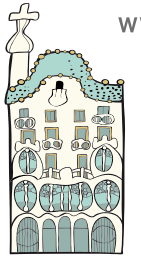
2017 BANFF-SCT
Joint Scientific Meeting

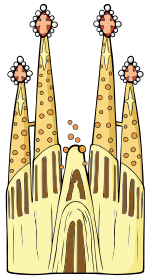
BARCELONA
27-31 March 2017

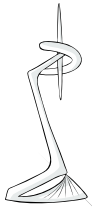


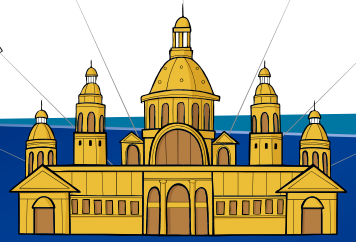
Societat Catalana de Trasplantament and
BANFF Foundation for Allograft Pathology
are pleased to co-host the
2017 Banff-SCT Joint Scientific Meeting

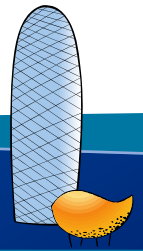
www.sctransplant.org
www.banfffoundation.org











Current transplant protocols reach fewer than 10% of those in need.

ONT
World Health Organization
GODT 2014

Global Activity in Organ Transplantation
2014 Estimates

Kidney	Liver	Heart	Lung	Pancreas	Small bowel
79948	26151	6542	4689	2328	215

≈ 119,873 solid organs reported to be transplanted in 2014

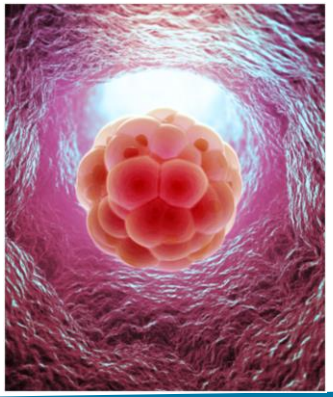
≈ 1.81 % of increase over 2013

≤ 10% of global needs

41.6% of living kidney transplants and 19.8% of living liver transplants

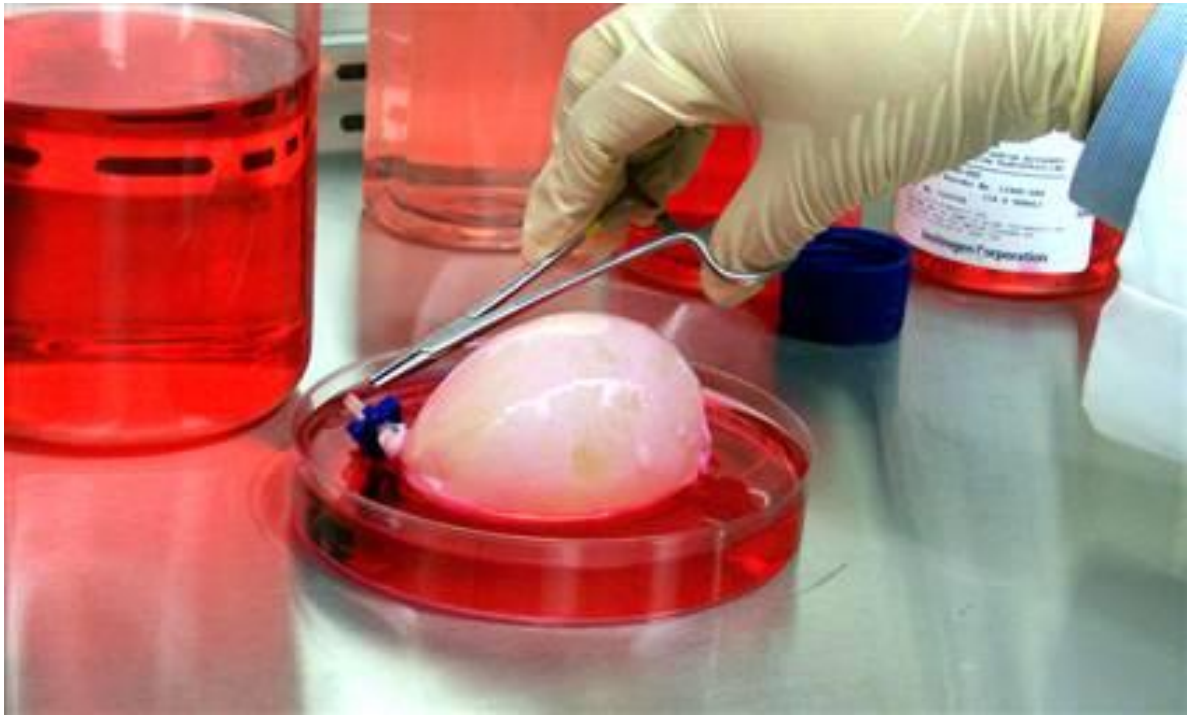
Information of 107 Member States on organ transplantation activities is included in the **GODT**: 93 of 2014, 6 of 2013, 2 of 2012, 3 of 2011 and 3 of 2010.

Worldwide 1.2 million people are in need of transplantation for end stage organ failure. Current transplant protocols reach fewer than 10% of this number. Regenerative medicine can save the remaining 90%, over one million people annually!

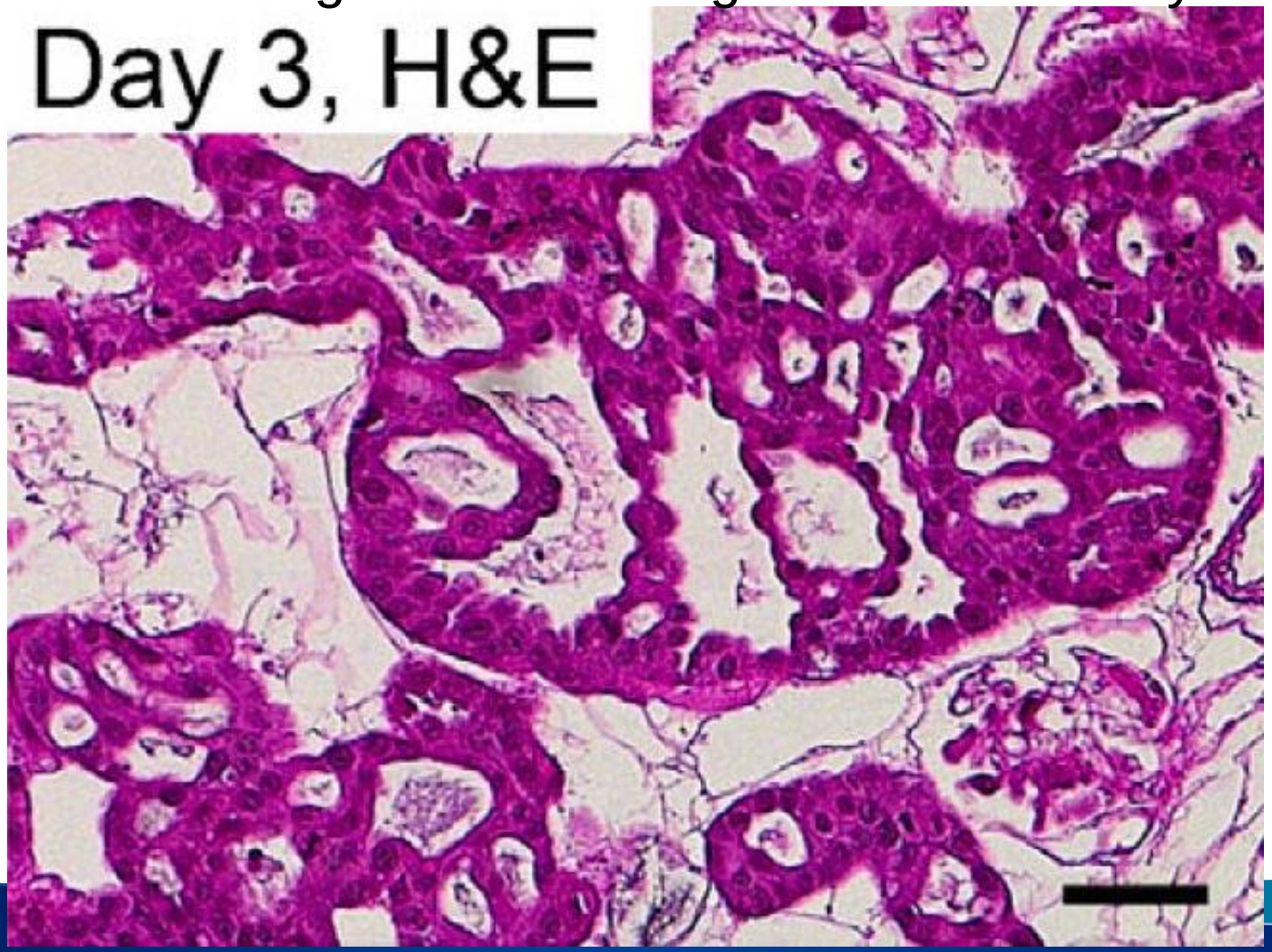


Regenerative Medicine Already Here! Working for Tubular Organs, Bladder, Trachea, Esophagus, Vagina.

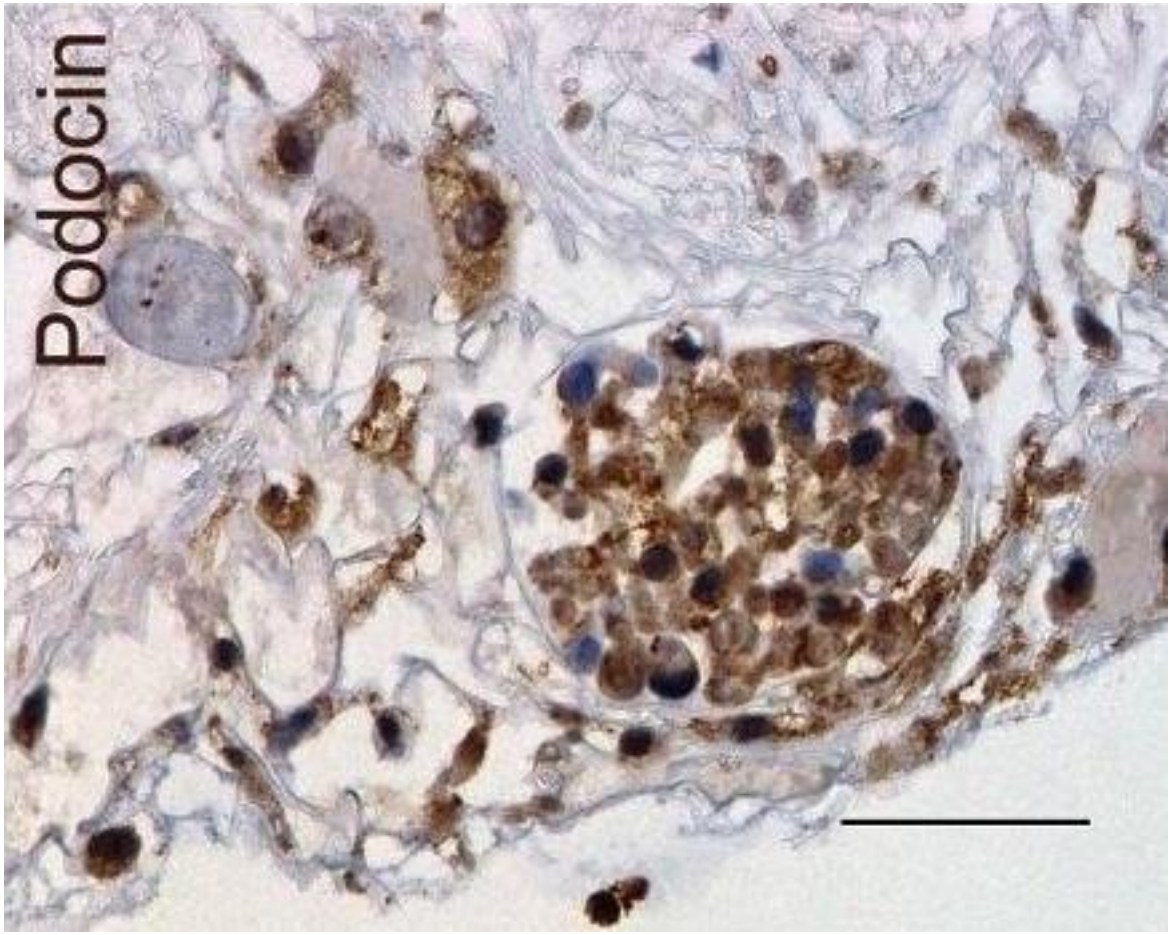
- Tissue engineered bladder.



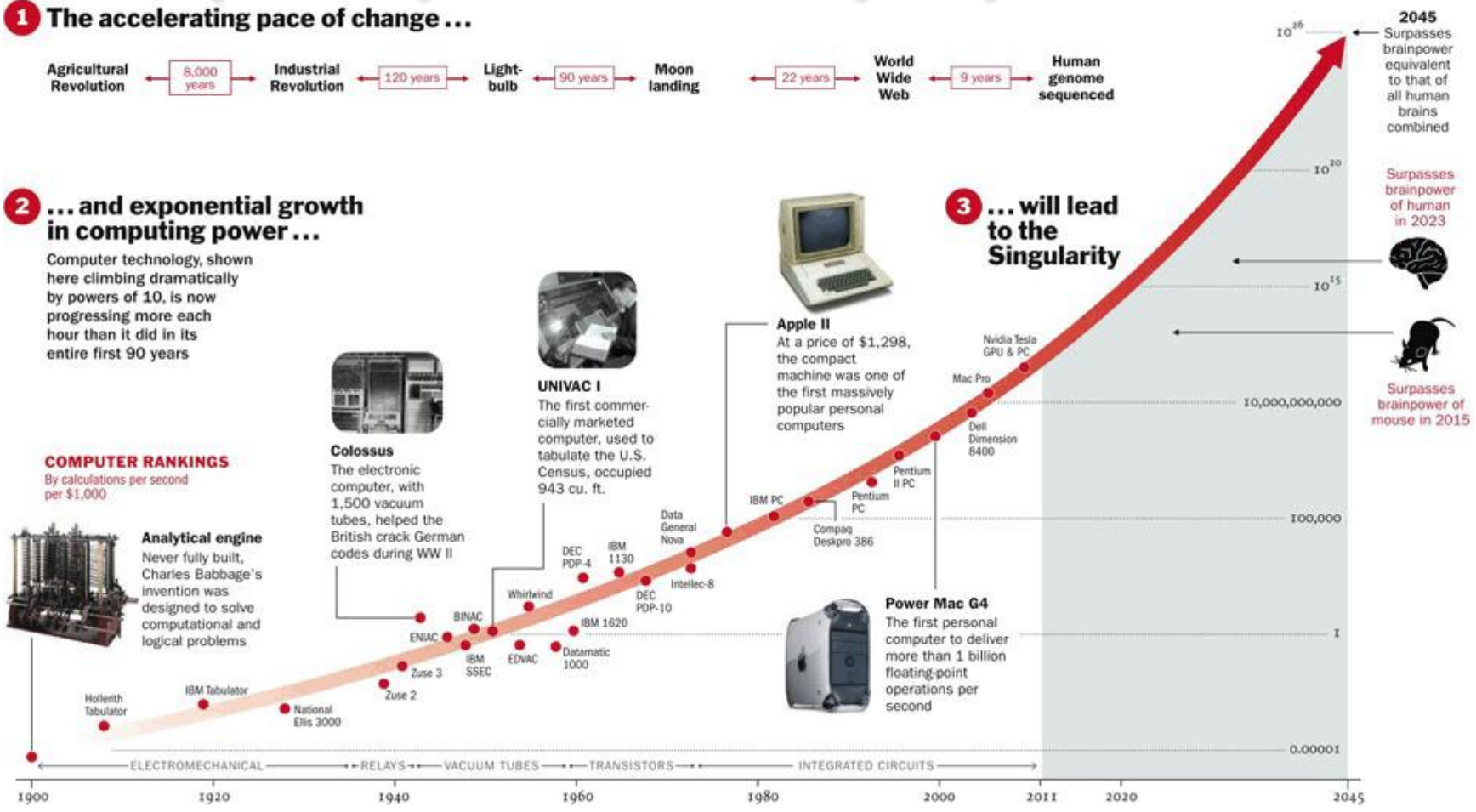
Song et al. Interstitium, vessels, and glomeruli with missing cells. Disordered tubule formation with multiple interconnecting lumina of differing sizes in bioengineered rat kidney.



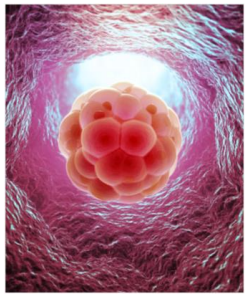
Song et al. In addition to missing cells and disordered structures, you have cells in the wrong places. Podocytes in the interstitium.

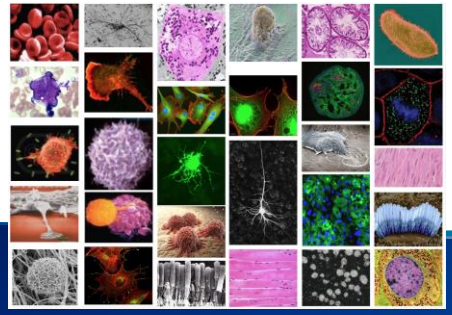


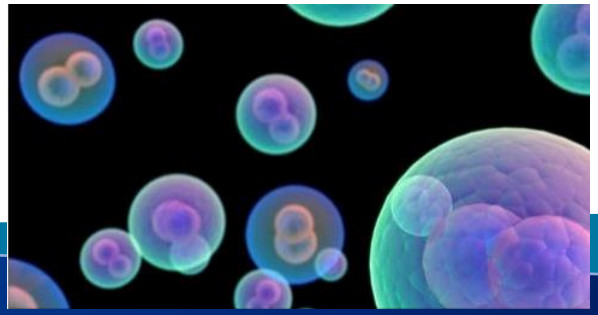
Nephrologists & Renal Pathologists May Be Only People Still Employed in 2045!



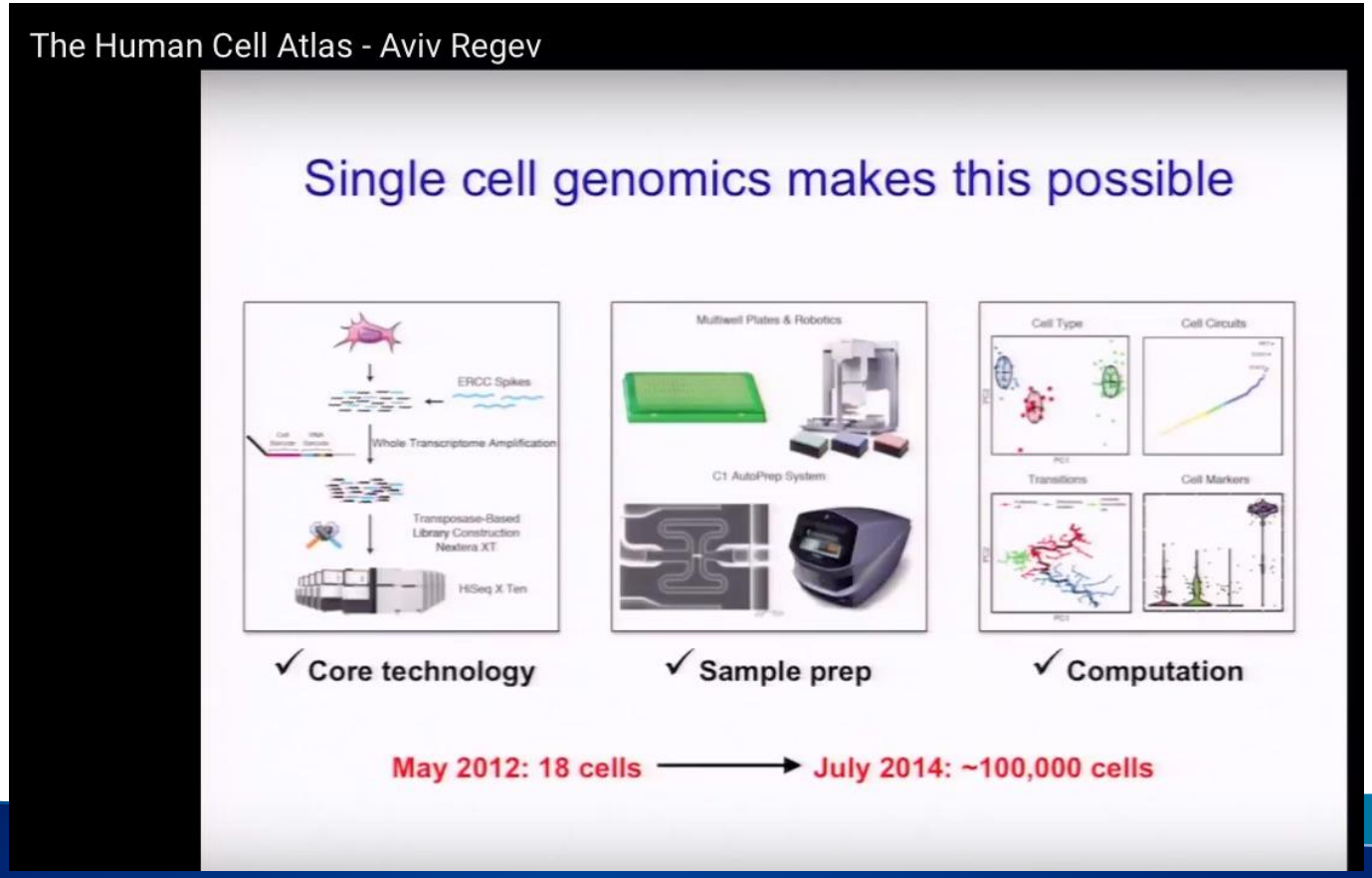
At the Banff meetings between the years 2011 and 2015 I introduced you to the concept of tissue engineering pathology. Today I introduce you to the idea the Human Cell Atlas project, the sequel to the Human Genome Project, as the future context of tissue engineering pathology.



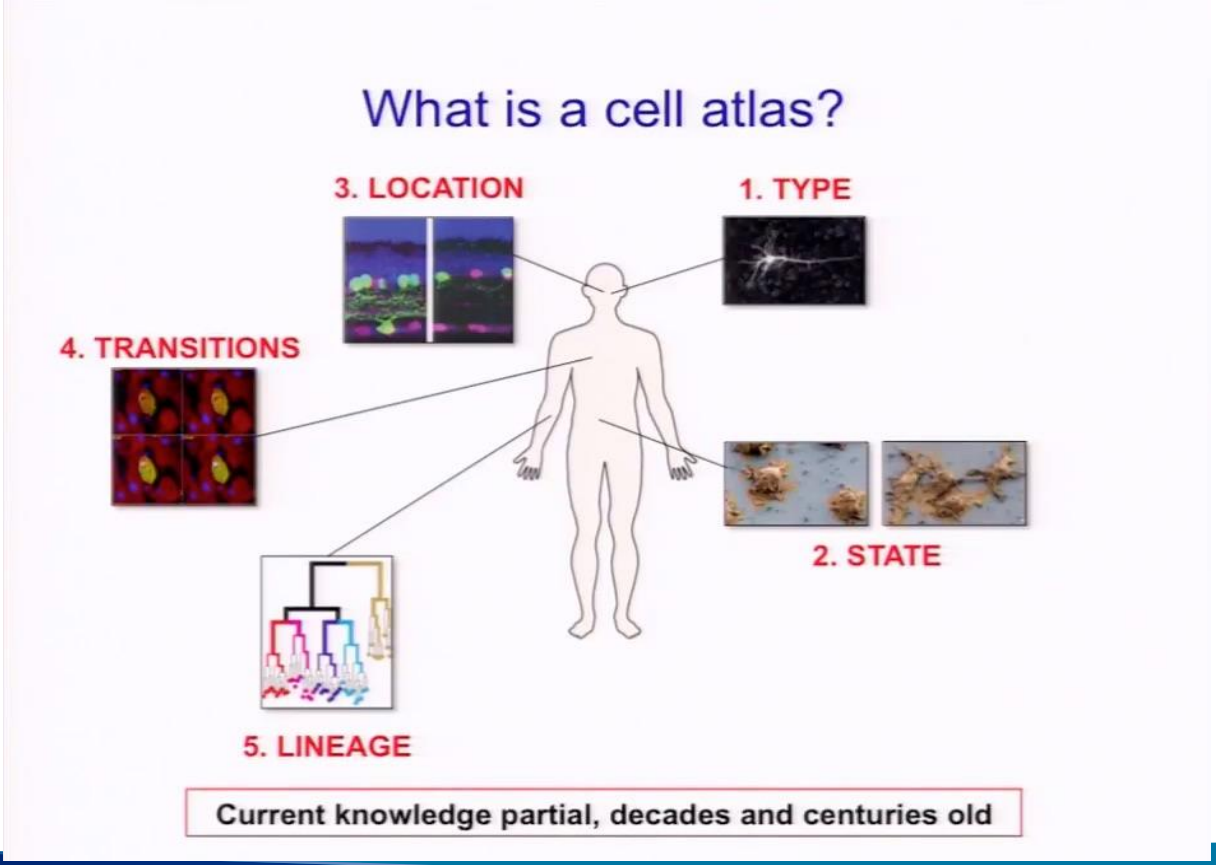




Something Missing In the Concept of Tissue Engineering Pathology: The Numbers – How Many Cells – How Many Conditions Can Be Treated



Aviv Regev's Human Cell Atlas Begins to Answer This: 300 Main Cell Types in Human Body – 20 in Kidney

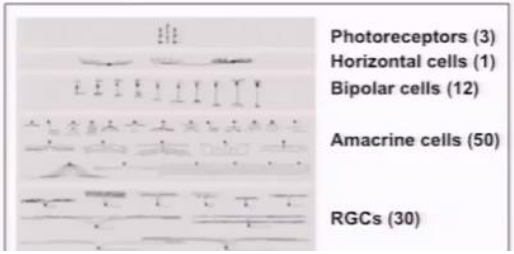


Aviv Regev's Human Cell Atlas Begins to Answer This: 300 Main Cell Types in Human Body – 1000s of subtypes

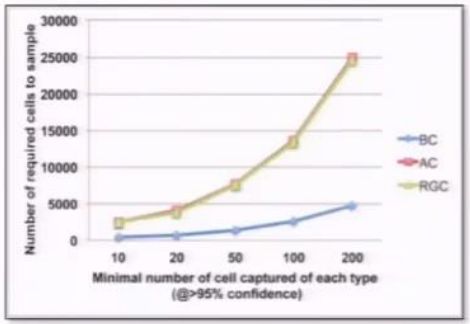
The Human Cell Atlas Project

Large

- Adult human: ~2X10^{13} cells (excluding red blood cells)
- 300 'major' cell types
- ….but, ~100 sub-sub-types just of retinal neurons



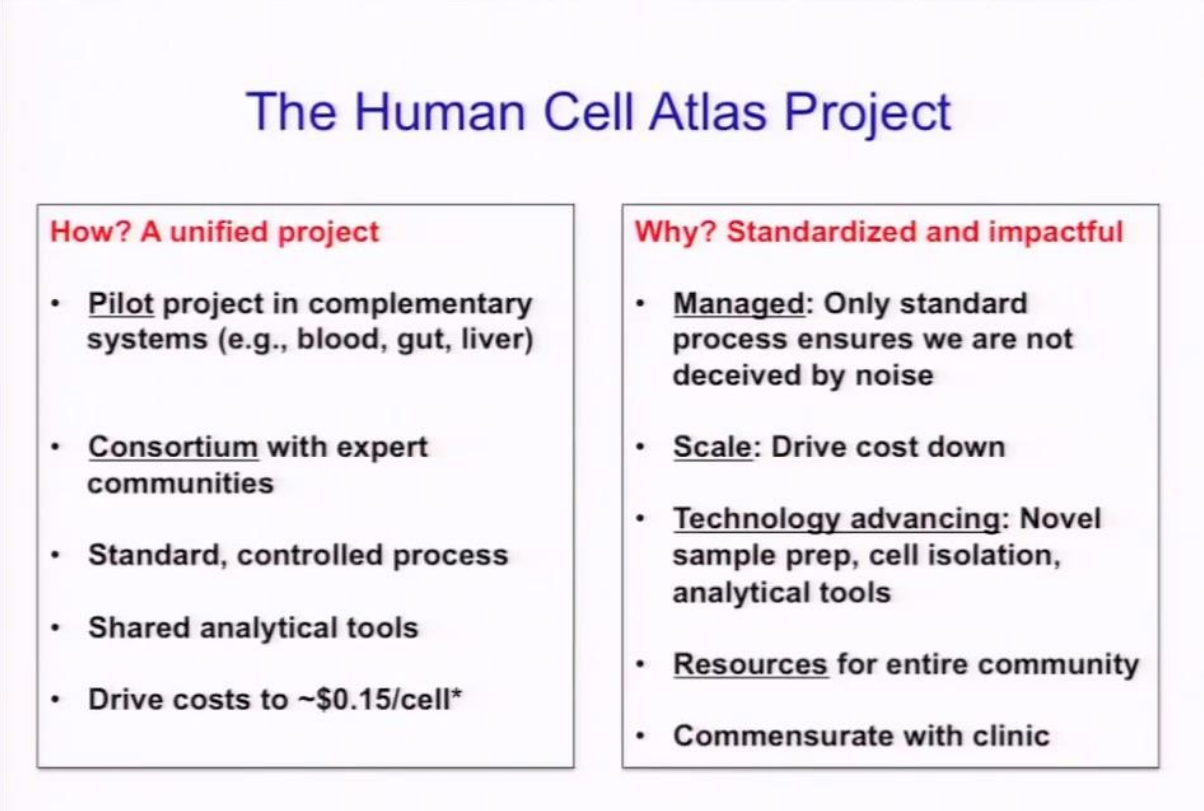
… but finite



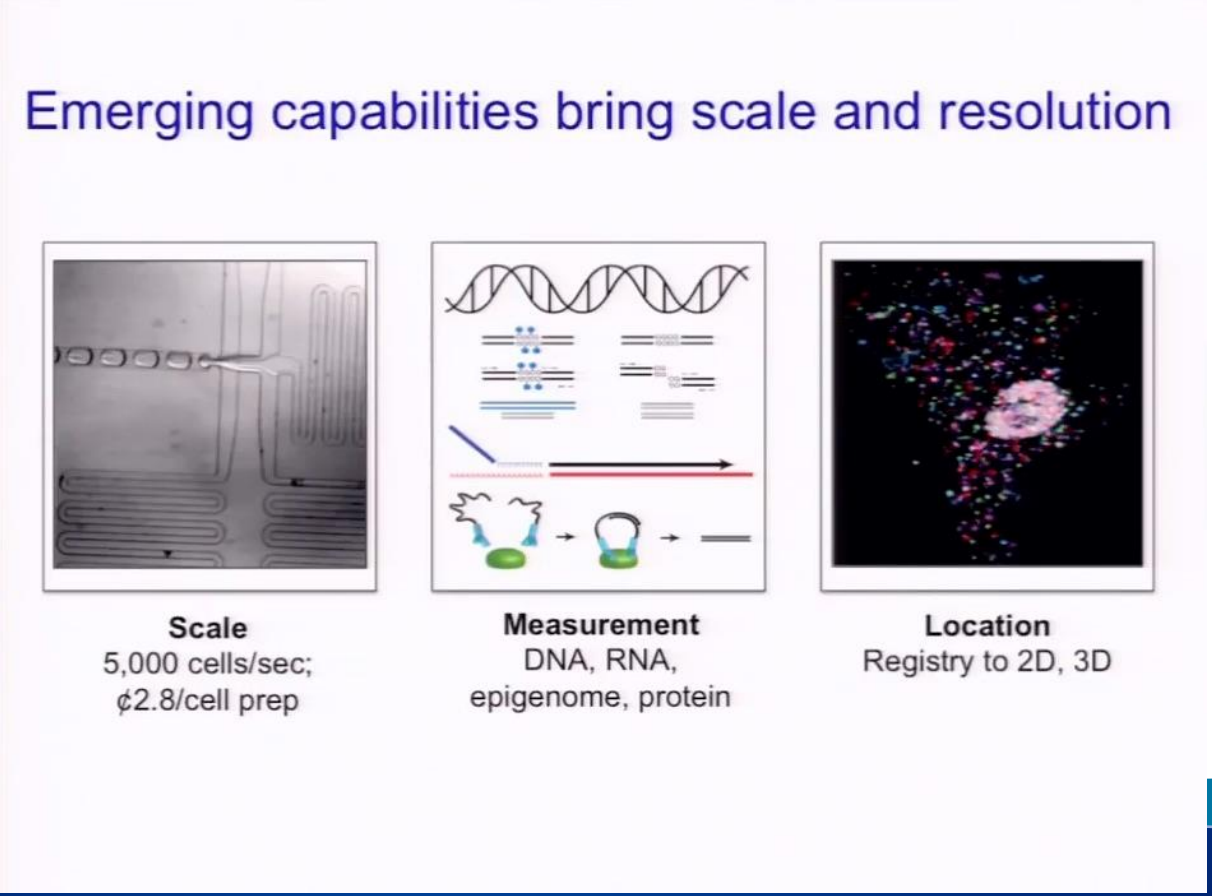
150M neurons in retina, ~40K required for survey

Retinal bipolar cell (BC): 12 sub types, rarest @5%
Retinal amacrine cell (AC): 50 subtypes, rarest @1%
Retinal Ganglial cell (RGC): 30 subtypes, rarest @1%

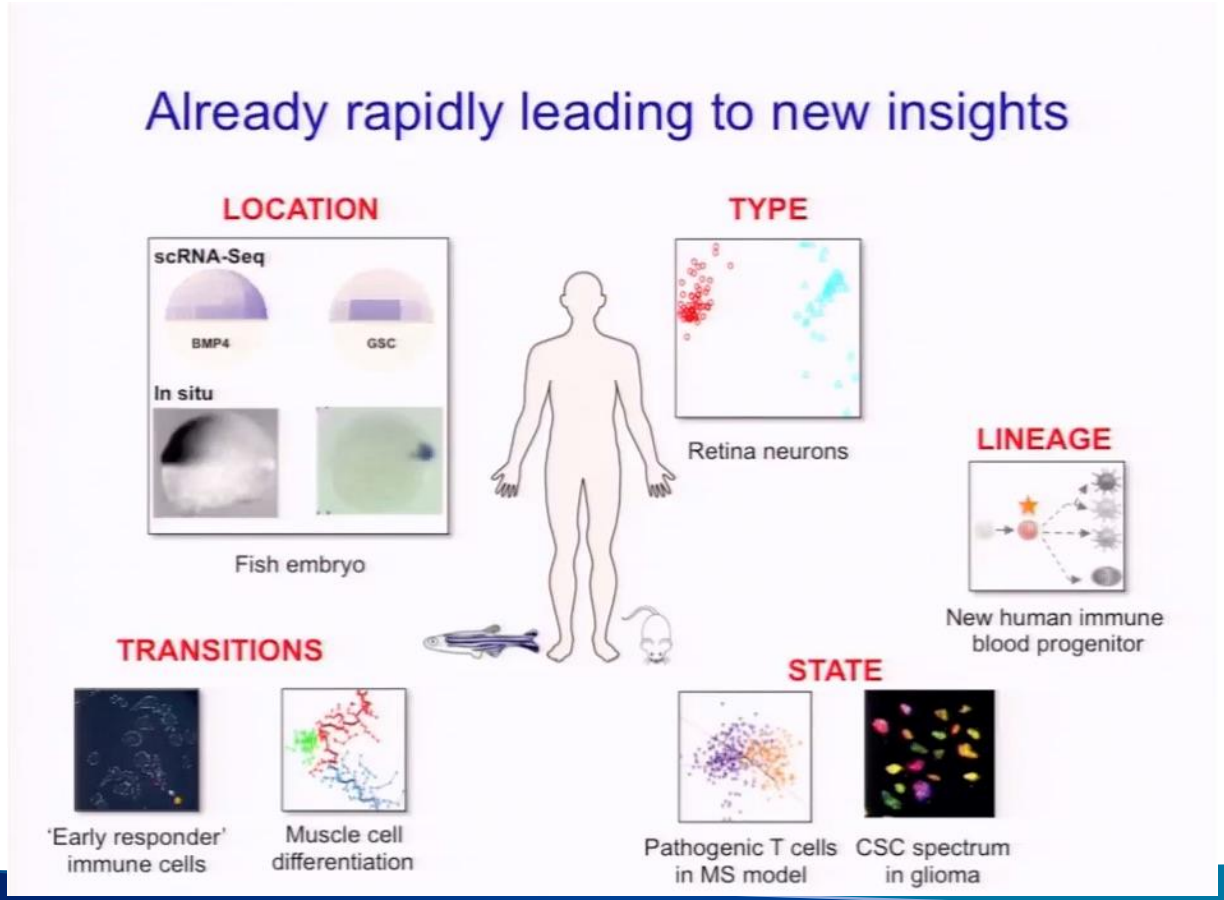
Aviv Regev's Human Cell Atlas Begins to Answer This Numbers Question: Analysis is Inexpensive and Fast



Aviv Regev's Human Cell Atlas Begins to Answer This Numbers Question: Analysis is Inexpensive and Fast, 5000 cells per second, 2.8 cents/cell.

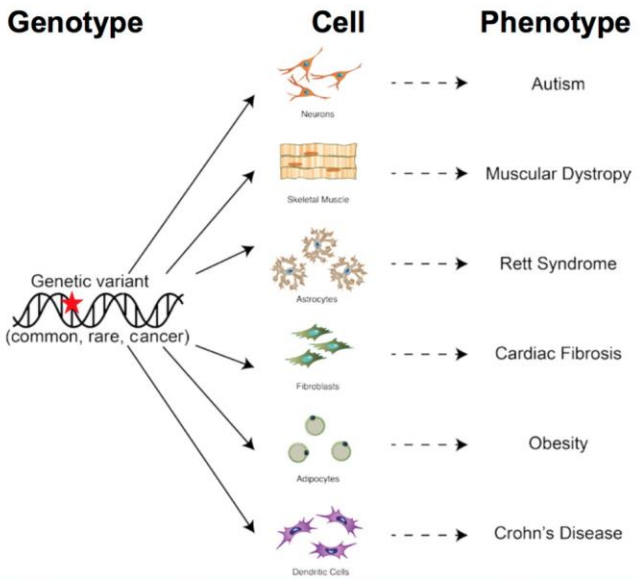


Aviv Regev's Human Cell Atlas Already Leading to Disease Insights Variants, Acting on Them = Pathology



Aviv Regev's Human Cell Atlas Already Leading to Disease Insights Variants, Acting on Them = Pathology

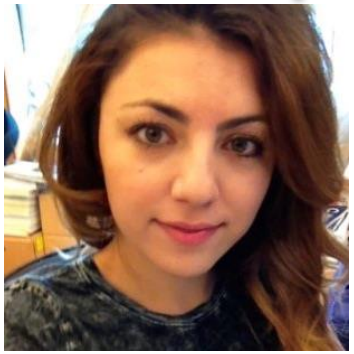
Cells: a key intermediate from genotype to phenotype

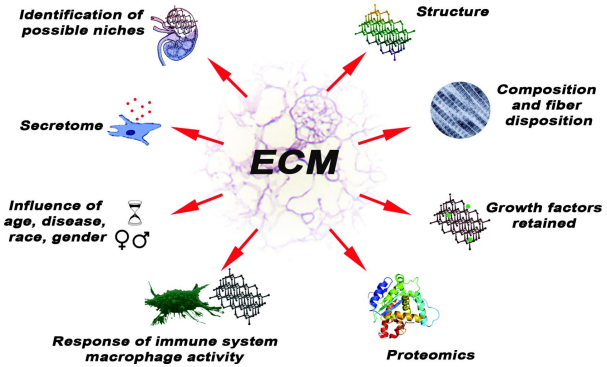


Knowing our cells is essential for functional dissection of genetic variants

Khouloud Saliba and I Presented Tissue Engineering Pathology at TERMIS Meeting in San Diego Dec. 11-14, 2016.

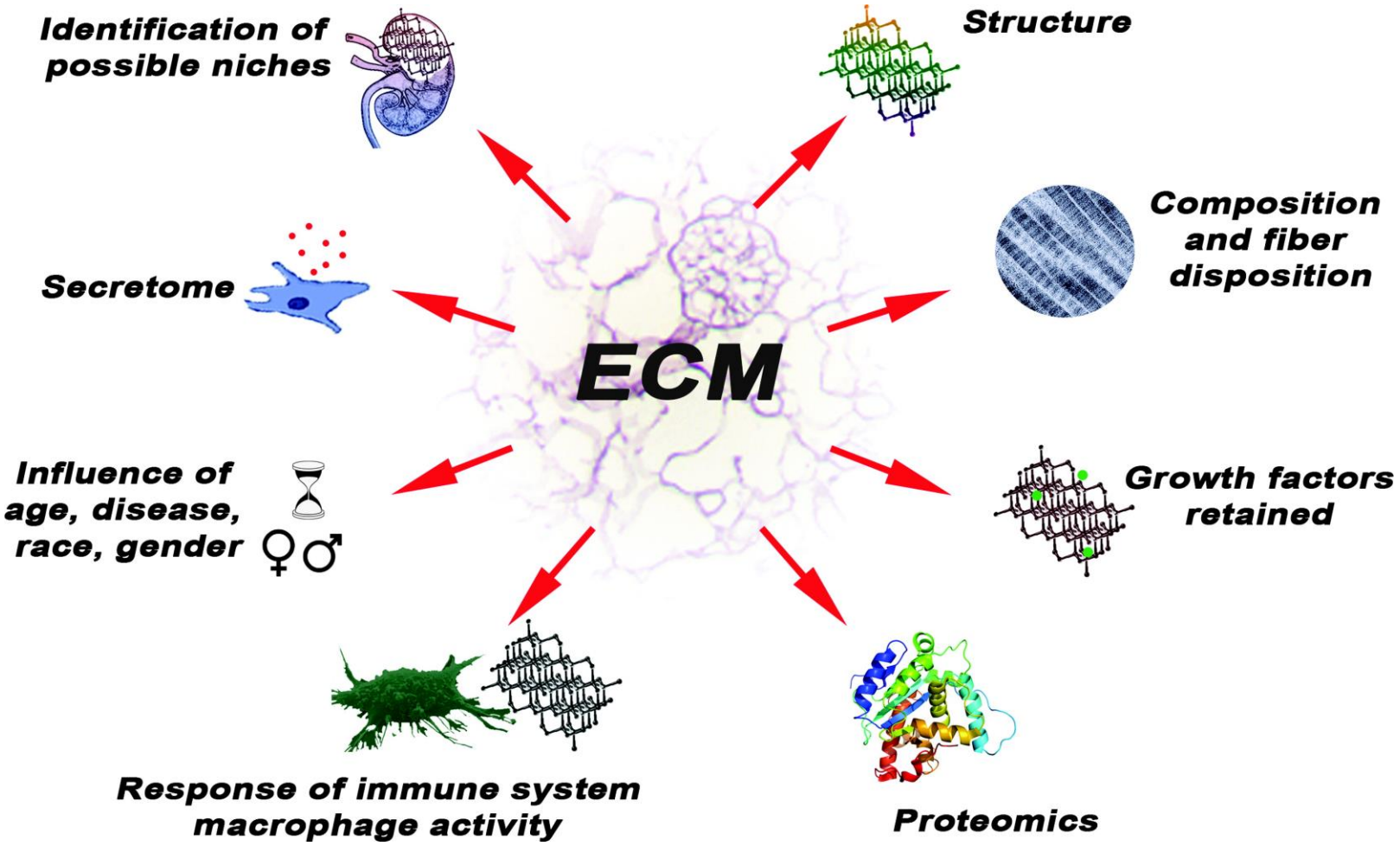
Met Astgik Petrosyan Who Has Written About the Many Additional Variables Which Will Add Complexity to New Banff Classification





- **Decellularized Renal Matrix and Regenerative Medicine of the Kidney: A Different Point of View** Petrosyan Astgik, … and Perin Laura. Tissue Engineering Part B: Reviews. May 2016, 22(3): 183-192.
- **A Step Towards Clinical Application of Acellular Matrix: A Clue from Macrophage Polarization.** Petrosyan A, …Perin L. Matrix Biol. 2016 Aug 26. pii: S0945-053X(16)30133-0.

Petrosyan … Perin Variables Will Necessitate AI Approaches to New Banff Classification!



Originally we had mule deer poking their heads into the meeting rooms. Now we have complex data requiring AI but outcome should be very good for patients. We've come a long way!

AI in Pathology: From Water Carriers to Purveyors of the Finest Wine!

FOLIA HISTOCHEMICA
ET CYTOBIOLOGICA
Vol. 47, No. 3, 2009
pp. 355-361

Review article

AI (artificial intelligence) in histopathology – from image analysis to automated diagnosis

Klaus Kayser[1], Jürgen Görtler[2], Milica Bogovac[1], Aleksandar Bogovac[1], Torsten Goldmann[3], Ekkehard Vollmer[3], Gian Kayser[4]

[1]UICC-TPCC, Institute of Pathology, Charite, Berlin, Germany
[2]DeepComputing, IBM, Antwerpen, Belgium
[3]Department of Pathology, Research Center Borstel, Borstel, Germany
[4]Institute of Pathology, University Freiburg, Freiburg, Germany

"The implementation of a complete connected AI supported system is in its childhood. Application of AI in digital tissue – based diagnosis will allow the pathologists to work as supervisors and no longer as primary "water carriers". Its accurate use will give them the time needed to concentrating on difficult cases for the benefit of their patients."

AI in Pathology: From Water Carriers to Purveyors of the Finest Wine!

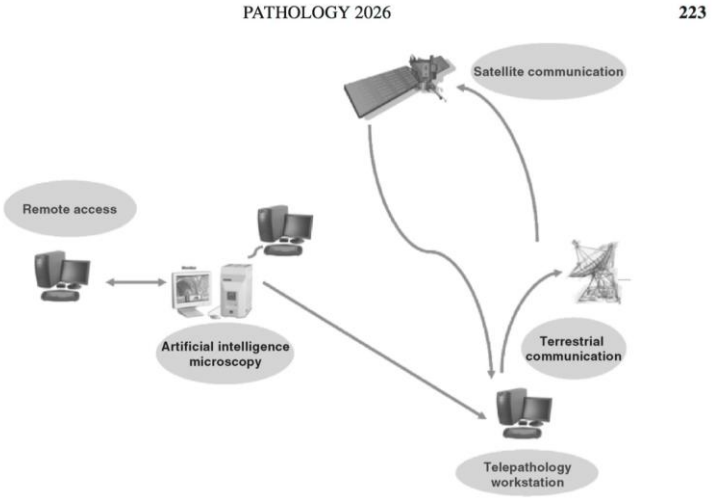
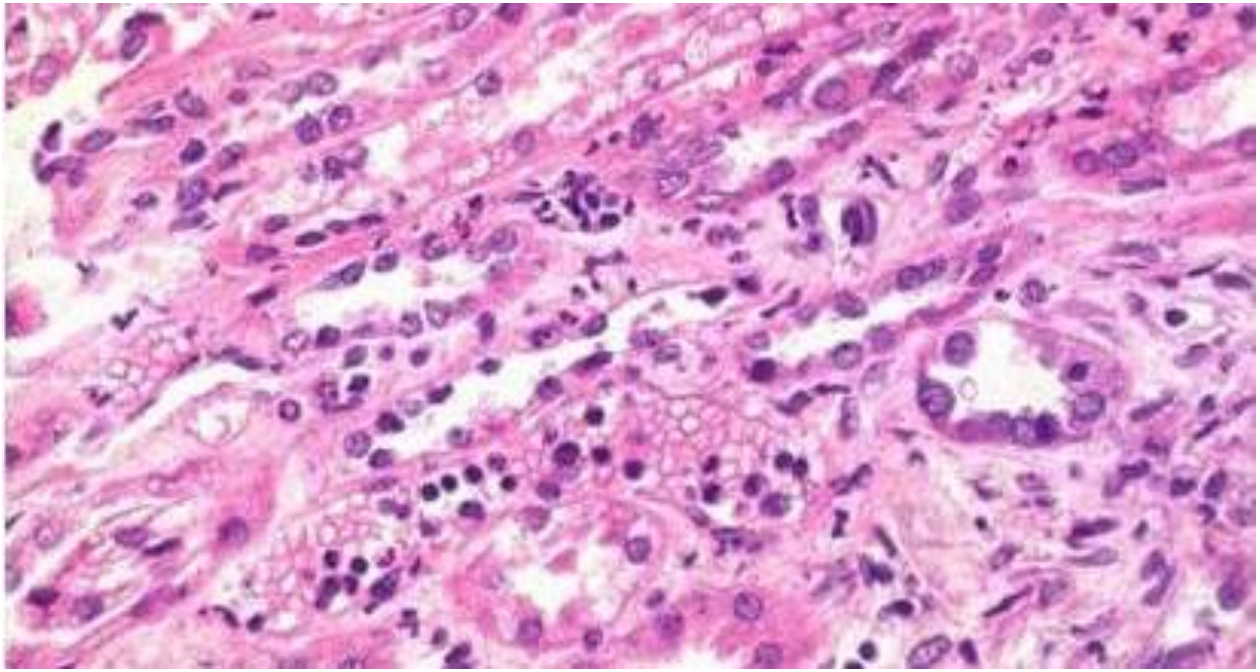


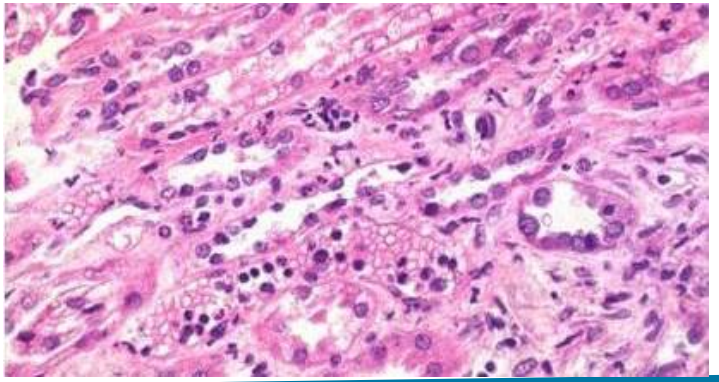
Figure 18.2 Reporting schema for cellular science in 2026, including use of artificial intelligence microscopy (AIM) and terrestrial and satellite communication.

- **Understanding Disease: A centenary celebration of the Pathological Society of Great Britain and Ireland, 2006, Chap. 18 Pathology 2026: The Future of Laboratory Medicine and Academic Pathology** *J.J. O'Leary*

Beginning at the beginning. My interest in transplant pathology began as an extension of my interest in transplant acute tubular injury (ATI) from studies of native kidney ATI.



Solez, Morel-Maroger, and Sraer Medicine 58:362-376, 1979. Morphology of "acute tubular necrosis" in man: Analysis of 57 renal biopsies and comparison with the glycerol model. My most cited paper before coming to Edmonton.



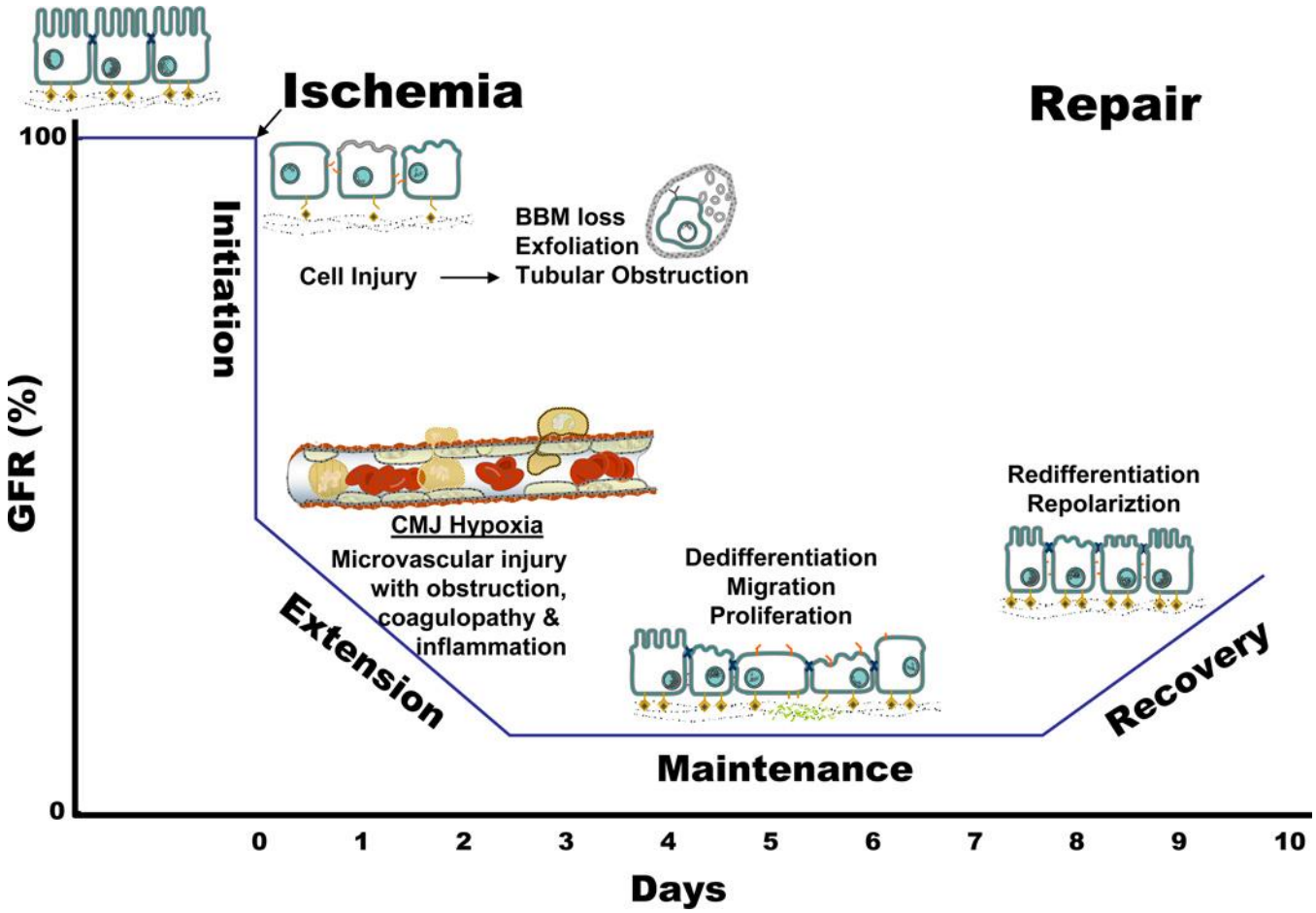
Solez, Morel-Maroger, and Sraer Medicine 58:362-376, 1979

1. *Of the 12 lesions assessed in the 57 "ATN" biopsies 10 persisted after functional recovery. Only 2 lesions correlated with function, were present when renal failure was present and absent after recovery: 1)Thinning of PAS positive brush border, & 2) shedding of individual tubular epithelial cells leaving bare basement membrane.*
2. *Lesions which persisted after recovery of function included tubular dilation, regeneration, mitoses, casts, interstitial edema, inflammation, nucleated cells in vasa recta, dilation of Bowman's capsule, tubularization of Bowman's capsule epithelium, & juxtaglomerular apparatus hyperplasia. The latter two were more prominent in recovery biopsies.*

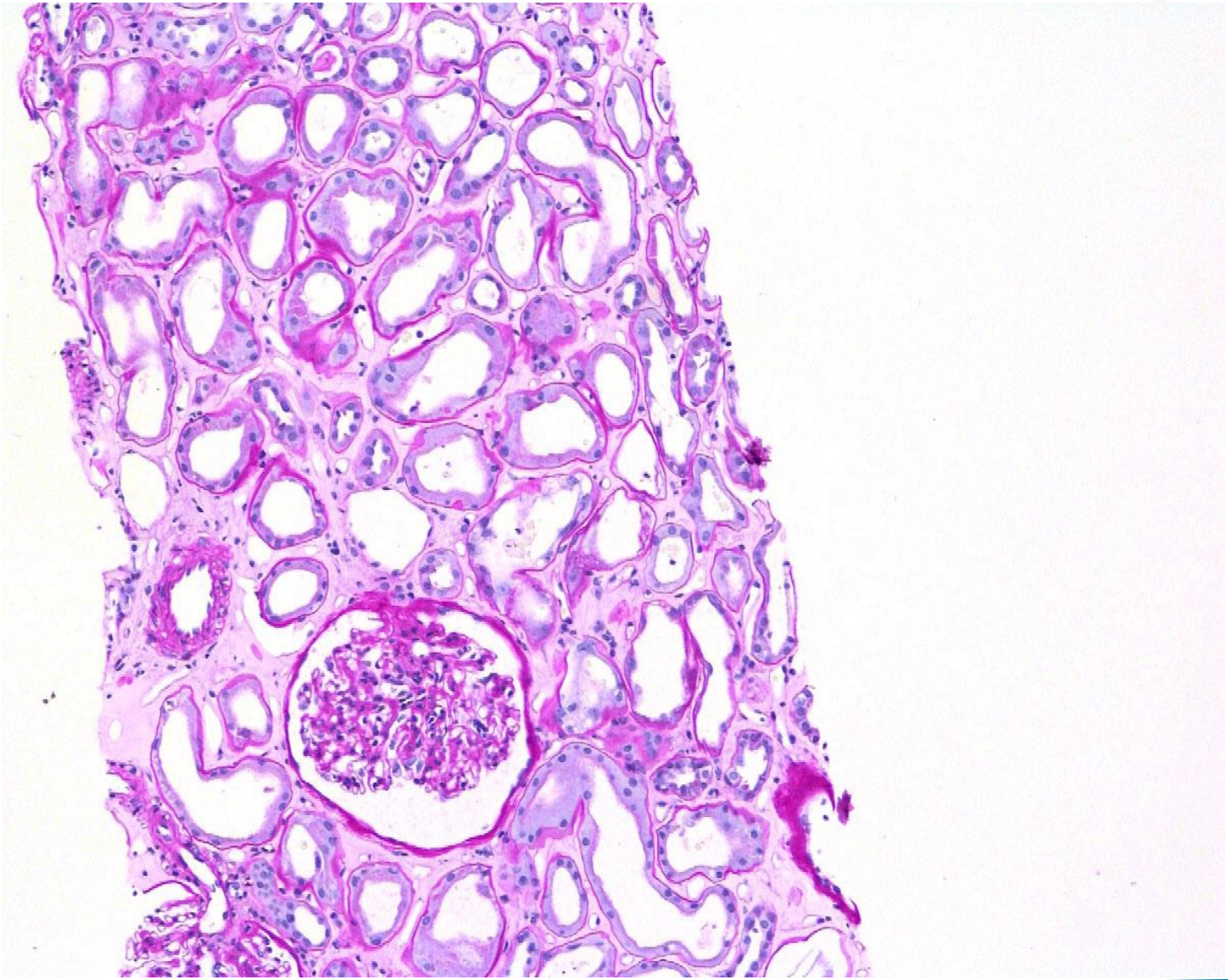
Solez, Morel-Maroger, and Sraer Medicine 58:362-376, 1979

1. *The two lesions which correlated with function, 1)Thinning or absence of PAS positive brush border, & 2) shedding of individual tubular epithelial cells leaving bare basement membrane, can be shown experimentally to occur within 5-15 minutes of reflow after an ischemic insult. They are as quickly reactive as molecular changes. Venkatachalam et al. Kidney Int. 1978; 14:31-49.*
2. *Lumping all acute tubular injury lesions together guarantees that histology assessment will appear to be inferior to molecular assessment, since the majority of ATI lesions persist after functional recovery. Only studies which separately assess the two lesions which correlate functionally are valid.*

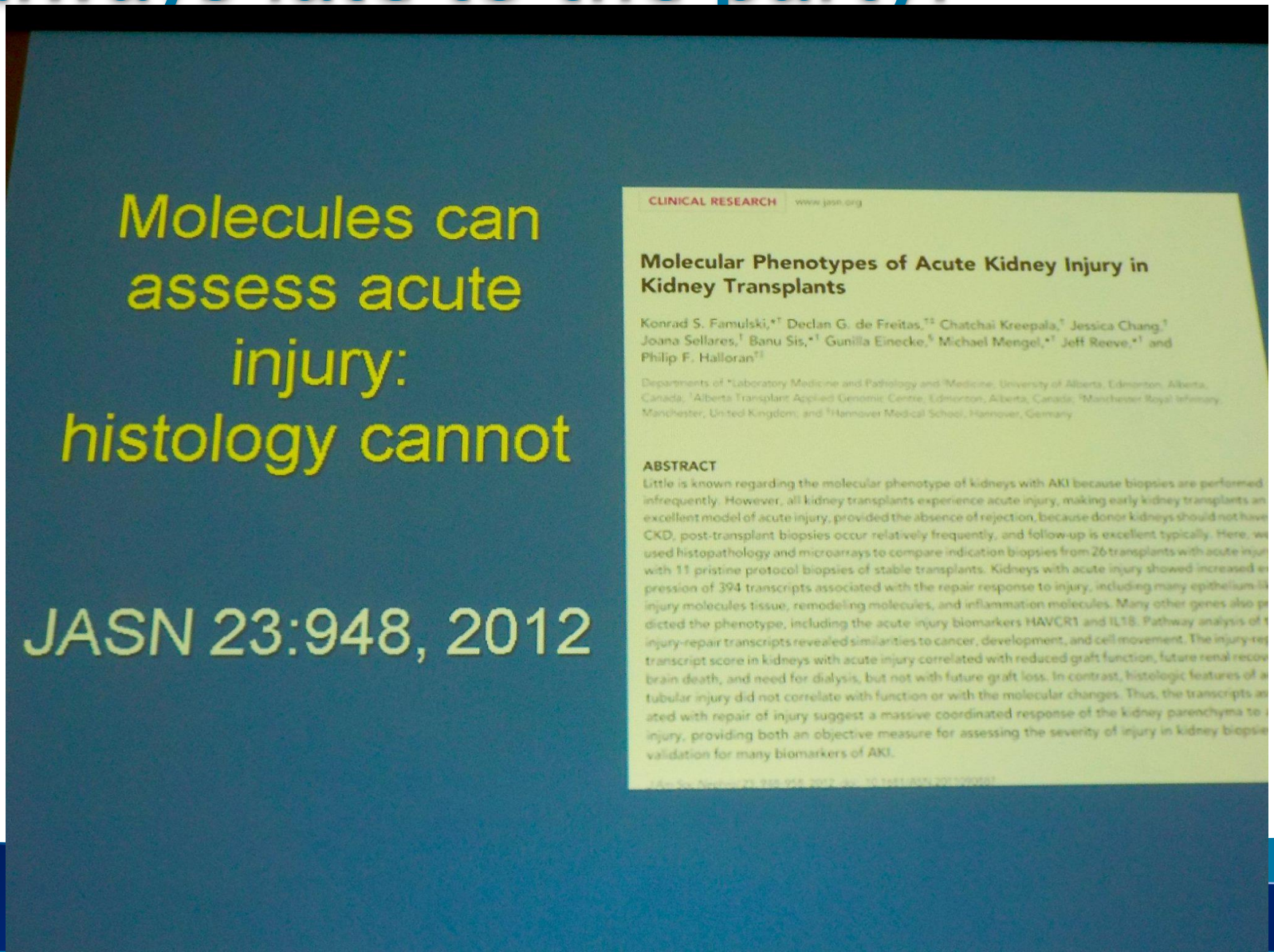
These papers are still referred to in recent reviews.



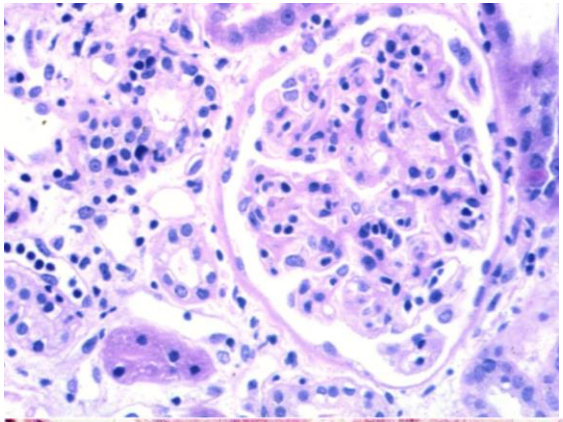
Still relevant to 2017 ATI recovery cases!

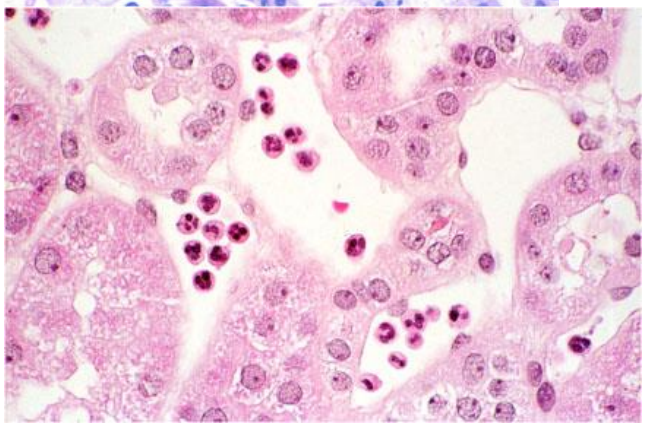


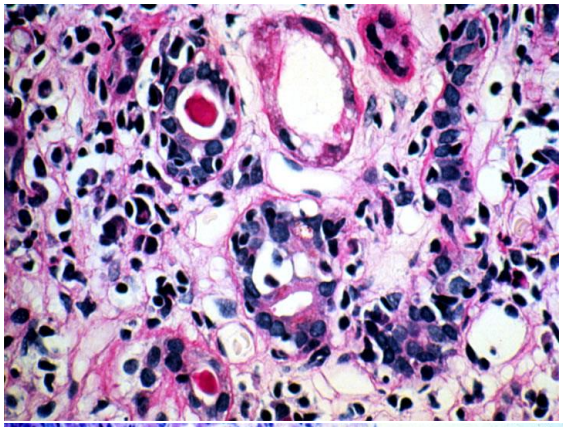
Not true that pathologists are always late to the party!

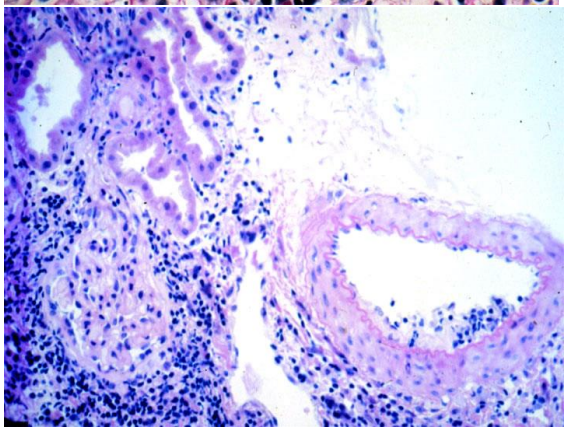


Banff Classification of Kidney Transplant Pathology









Histologic criteria for the diagnosis of rejection and other conditions in the transplanted kidney, began 1991, updated and expanded every two years in consensus meeting.

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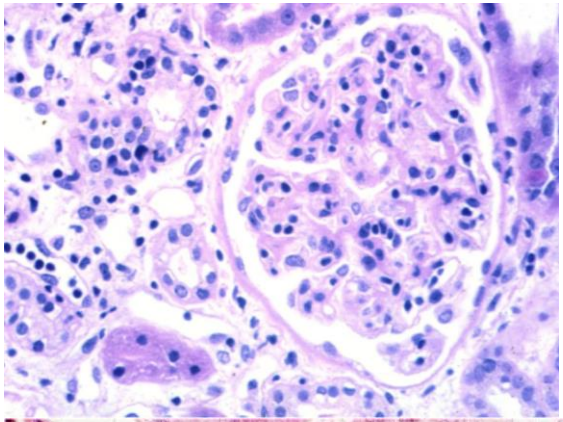
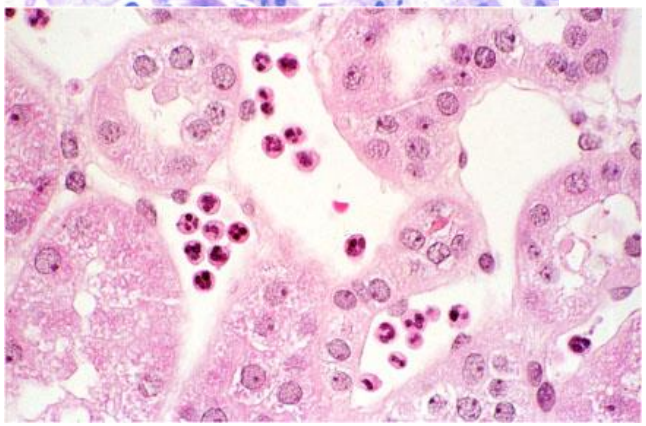
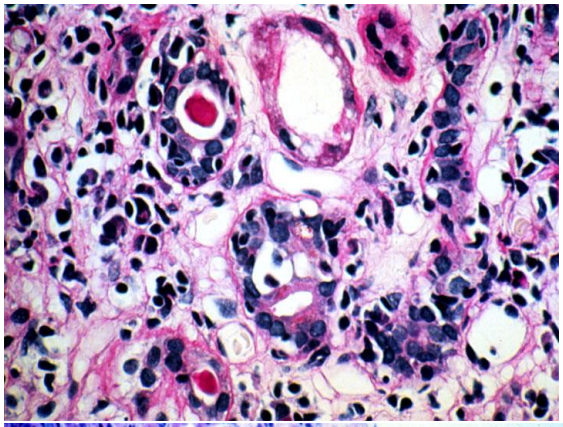
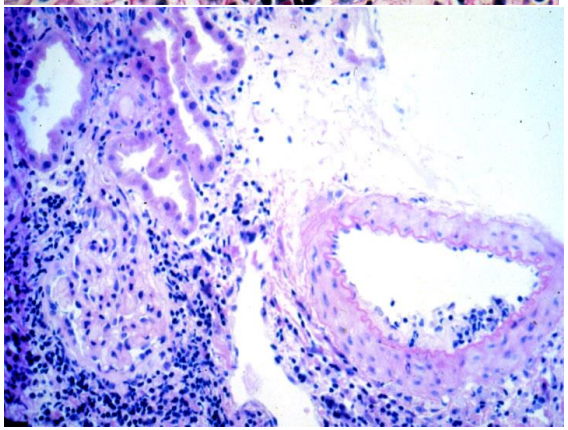
Banff Lesion Scoring:Sign of Educated Tx Pathologist









imprimatur 1. The formula (='let it be printed'), signed by an official authorizing printing of a book;hence as *sb.* an official license to print.

The Oxford English Dictionary (2nd. ed.)

Banff lesion scoring: g cg i ci t ct v cv ah mm ptc C4d

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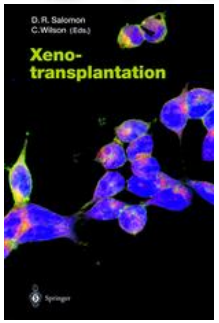
Where Did the Lesion Scoring Thresholds Come From?

1. *In the beginning they were based on our experience with protocol transplant biopsies from Baltimore, Edmonton, Paris, and Aarhus from the years 1983 to 1991, but then modified by practical considerations of what one could do in the 29 minutes examination of a complex surgical pathology case was supposed to not exceed, and by our experience using cases in training workshops from 1991 to 1999. In the early Banff meetings there were always microscopes there.*
2. *Two of the most memorable training workshops were held at the University of Basel and hosted by Michael Mihatsch. They contributed a lot to finalizing lesion scoring ideas.*

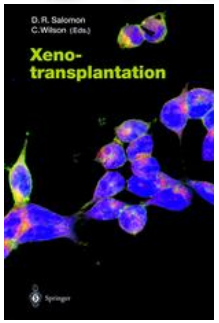
Daniel R. Salomon, M.D. 1953-2016 A Legend in His Own Time – A Tribute

- Date: Mon, 21 Nov 94 09:00:29 PST
- To: NEPHROL From: dsalomon@scripps.edu (Daniel R. Salomon, MD) A lesion that Byron Croker and I found very interesting ... was the presence of a peritubular capillary lymphocytic infiltrate .... The presence of the peritubular capillaritis was associated with rejection in over 50 cases we biopsied for delayed graft function within 10 to 14 days post transplantation and also appeared in biopsies of some patients with otherwise classic acute tubulointerstitial rejection at later time points.
- Should these lesions be studied in the context of the Banff Schema? Daniel Salomon, MD

Daniel R. Salomon, M.D. 1953–2016 A Legend in His Own Time – A Tribute



Daniel R. Salomon, M.D. 1953–2016 A Legend in His Own Time – A Tribute



Students and I Returned to the Site of Famous New Orleans Court of Two Sisters NEPHROL Dinner of Nov 2 1996 19 Years Later in 2015

Daniel R. Salomon, M.D. 1953–2016 A Legend in His Own Time – A Tribute

- He defied categorization, had very broad interests, with important impact all over the spectrum from basic research to high impact clinical work and health policy. We had a longstanding agreement that he would take over the running of NEPHROL if anything happened to me.
- He insisted that the correct term was ”regenerative medicine transplantation” that the word ”transplantation” should not be lost. Bioengineered organs still fit within the term ”transplantation”.
- He strongly supported the AST CEOT meetings when there were efforts made to eliminate them.

Daniel R. Salomon, M.D. 1953–2016 A Legend in His Own Time – He Will Be Greatly Missed!