

Petite histoire de la transplantation hépatique

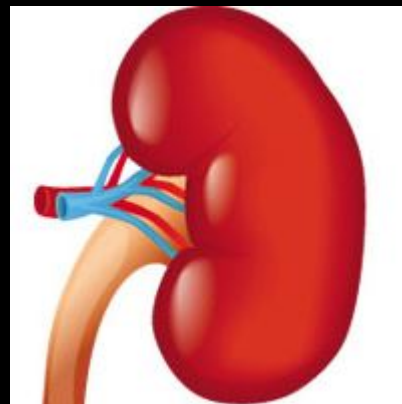
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1950-1980

L'ère des pionniers de la greffe

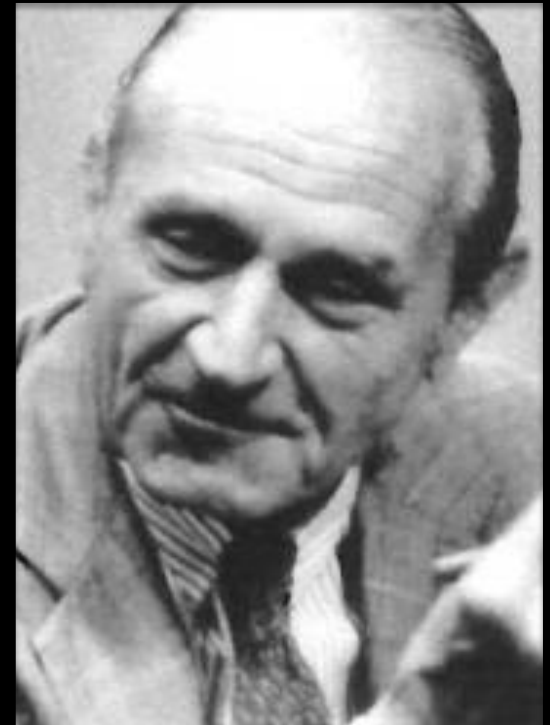
Le rein d'abord





1947 David Hume
1^{ère} allogreffe de rein
« en toute discrétion »

Les pionniers de la greffe rénale



Joseph Murray, Jean Hamburger, René Kuss

Table 1

Kidney Transplantation: Survival of 6 Months or More as of March 1963 (Above Dot)

Patient No.	City (Ref)	Date	Donor	Survival (mo)
1	Boston (⁴⁰)	1-24-59	Fraternal twin	>50
2	Paris (⁴¹)	6-29-59	Fraternal twin	>45
3	Paris (⁴²)	6-22-60	Unrelated*	18 (died)
4	Paris (⁴¹)	12-19-60	Mother*	>12 (died)
5	Paris (⁴²)	3-12-61	Unrelated*	18 (died)
6	Paris (⁴¹)	2-12-62	Cousin*	>13
7	Boston (⁵⁴)	4-5-62	Unrelated	11

Boston: JE Murray (patients 1 and 7).

Paris: J Hamburger (patients 2, 4 and 6), R Kuss (patients 3 and 5).

* Adjunct steroid therapy.

Des malades trop graves

Une immunosuppression trop forte

Aplasiants médullaires

Irradiation corporelle totale

Corticothérapie fortes doses

Des greffons mal compris

Prélèvement

Implantation

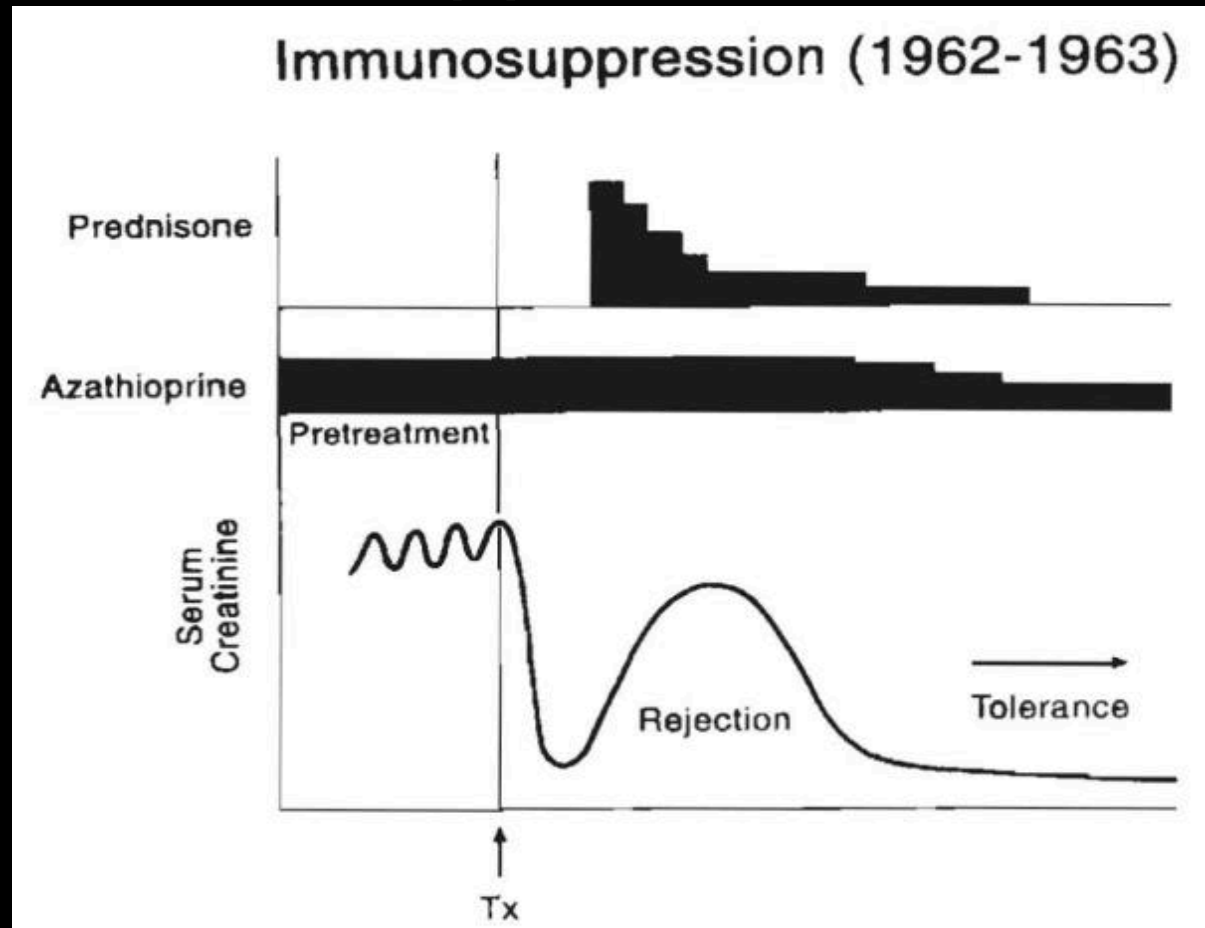
Des rejets « irréversibles »

1957 l'Azathioprine

Premiers « protocoles » d'immunosuppression

1 + 1 = 3

Le rejet n'est pas
une fatalité



Premieres tentatives Denver (Colorado)



Thomas Starzl
1927-2017

1963 : année miraculeuse



Première greffe de poumon, Jackson USA

Première greffe de pancréas, Minneapolis USA

Première greffe de foie, Denver USA

Première greffe d'intestin, Sao Paulo Br



Christiaan BARNARD
Cap Town 7/12/1967; 5h52 AM

L'essor de la greffe de foie

Premieres tentatives Denver (Colorado)



Thomas Starzl
1927-2017

Table 3

The First Seven Human Liver Recipients

Age (y)	Date	City (ref)	Liver disease	Survival (d)	Main cause of death
3	3-1-63	Denver ⁽⁶⁰⁾	Biliary atresia	0	Intraoperative bleeding
48	5-5-63	Denver ⁽⁶⁰⁾	Hepatoma, cirrhosis	22	Pulmonary emboli, sepsis
68	6-3-63	Denver ⁽⁶⁰⁾	Duct cell carcinoma	7.5	Pulmonary emboli
52	7-10-63	Denver ⁽⁶⁴⁾	Hepatoma, cirrhosis	6.5	Gastrointestinal bleeding, pulmonary emboli/edema, liver failure

Chirurgie difficile

Un postopératoire compliqué

Problèmes techniques

Problèmes immunologiques

Début des années 1980

Geste technique mal maîtrisé

Contrôle de la réaction immune difficile

Les risques de la greffe sont supérieurs aux bénéfices

Greffes = opération de la dernière chance
donc chances de succès faibles

Mais...quelques beaux succès... exceptionnels

Espoir des malades...et des chercheurs

Cellule du donneur



CD4

Lymphocyte T
auxiliaire du
receveur

Immunité de greffe

Anti lymphocytes

Premier signal

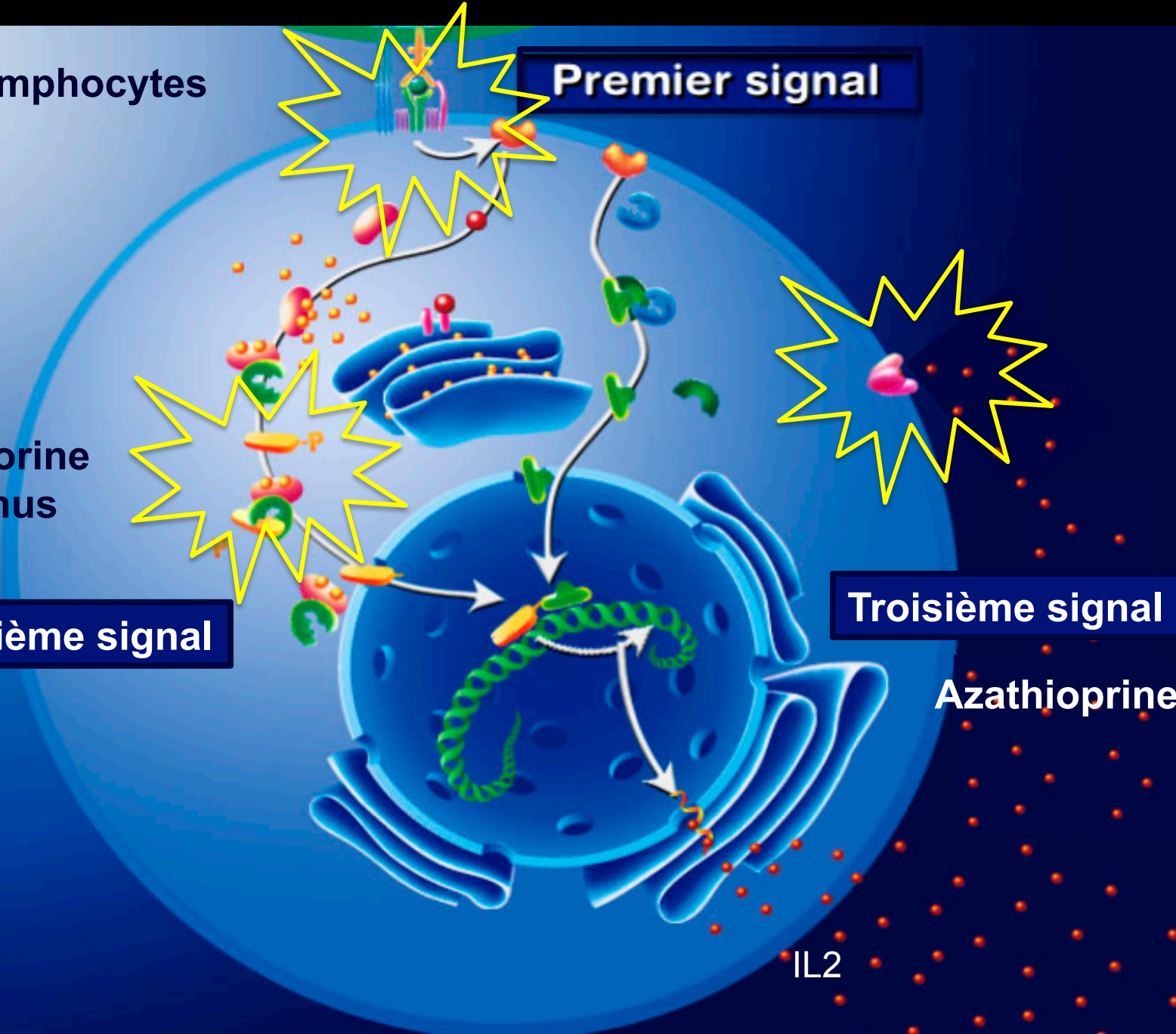
**Ciclosporine
Tacrolimus**

Deuxième signal

Troisième signal

Azathioprine

IL2



The Lancet

Saturday 23 & 30 December 1978

CYCLOSPORIN A IN PATIENTS RECEIVING RENAL ALLOGRAFTS FROM CADAVER DONORS

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S. THIRU
P. MCMASTER
G. N. CRADDOCK

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Diagnosis	No. of HLA-AB mismatches	Previous bilateral nephrectomy	Total ischaemia (min)	Previous blood-transfusions (in units)	Daily dose in mg/kg (CM=cyclosporin; P=prednisolone; d=day)	Outcome	
1. Glomerulonephritis	2	No	958	20 in preceding 18 mo	Cy A. 25 d0-11 20 d 12-14 17 d 15-21 12 d 22-27	Transplant nephrectomy day 28. Pyelonephritis in graft. On dialysis.	
2. Systemic lupus erythematosus	3	No	514	9 in preceding 18 mo	Cy A. 25 d0-12 20 d 13-15 15 d 16-18 10 d 18 continuing	Discharged on day 22.	
3. Malignant hypertension	4	Yes	348	4 in preceding 4 mo	Cy A. 25 d0-15 20 d 16-17 17 d 18-36 12 d 37 continuing	CM 2.0 d 10-28 1.5 d 29-30 1.0 d 31-36 0.5 d 37 continuing	Vascular rejection day 7. Recovered function. Discharged day 53.
4. Glomerulonephritis	3	No	583	5 in preceding 4 mo	Cy A. 25 d0-13 20 d 14-23 17 d 24-31 12 d 32-37 17 d 38-46 12 d 61 continuing as capsules from 64th day	CM 2.0 d 47-49 1.0 d 56 continuing P. 4.0 d 49-51 2.0 d 52 1.0 d 53-54 0.7-0.5 d 56-60 0.4 d 61-81 0.2 d 82 continuing	Discharged day 42.
5. Chronic pyelonephritis	3	Yes	368	4 in preceding 2 mo	Cy A. 25 d0-16 20 d 17-24 15 d 25-32 10 d 33-37 20 d 38-44 15 d 45-66 10 d 67-68 12 d 69 as capsules continuing	CM 1.0 d 50 continuing P. 4.0 d 42-44 2.0 d 45 1.0 d 46 0.5-0.1 d 47-53 0.4 d 54-66 0.3-0.2 d 67-72 0.1 d 73 continuing	Discharged day 78.
6. Malignant hypertension	2	No	215	3 in preceding 3 mo	Cy A. 25 d0-5 20 d 6-11 15 d 12-13 10 d 14-18 25 d 19-24 20 d 25-45 15 d 46 continuing	CM 1.0 d 71 continuing P. 4.0 d 21-23 2.0 d 24 1.0 d 25 0.5 d 26-40 0.4 d 41-48 0.3 d 49-51 0.2 d 52 continuing	Discharged day 56.
7. Malignant hypertension	2	No	75	3 in preceding 3 mo	Cy A. 25 d0-4 22 d 5-6 19 d 7-9 16 d 10-11 13 d 12-13 9 d 14-18 25 d 19-24 19 d 25-38 16 d 39-43 13 d 44-45	CM 2.0 d 41-43 1.0 d 44-45 P. 4.0 d 21-23 2.0 d 24 1.0 d 25 0.5 d 26-40 0.4 d 41-42 0.2 d 43 continued until death	Died day 55, disseminated aspergillosis

Liver transplantation

ACTUAL EIGHTEEN MONTH SURVIVAL OF 210 CONSECUTIVE RECIPIENTS

TREATMENT	NO.	TIME IN MONTHS				
		1	2	6	12	18
Triple Drug Conventional (1963 – 1979)	170	120 (58%)	95 (55.9%)	65 (33.2%)	56 (32.9%)	47 (27.6%)
Cyclosporine - Steroids (1980 – 1981)	40	32 (80%)	31 (77.5%)	29 (72.5%)	28 (70%)	26 (65%)

CONSENSUS CONFERENCE REPORT ON LIVER* TRANSPLANTATION

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Liver transplantation has been developed to the point of a service operation, the exploitation of which depends upon the establishment of multiple regional centers. The increased use of this procedure will permit the delivery of optimum health care to victims of end stage liver disease.

L'explosion



Fujimycine

Anti lymphocytes
Anti CD3
Anti CD4

Premier signal

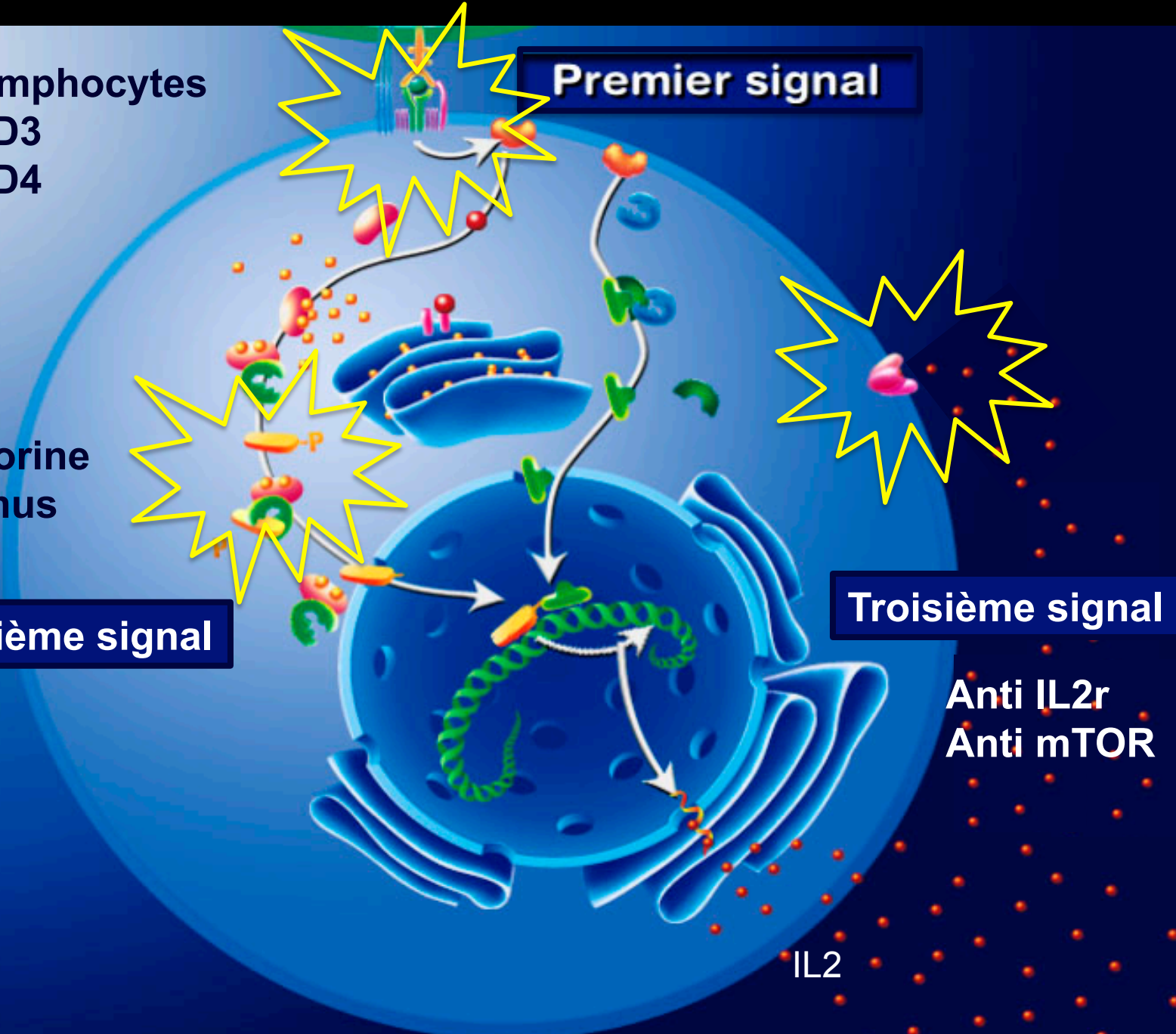
Ciclosporine
Tacrolimus

Deuxième signal

Troisième signal

Anti IL2r
Anti mTOR

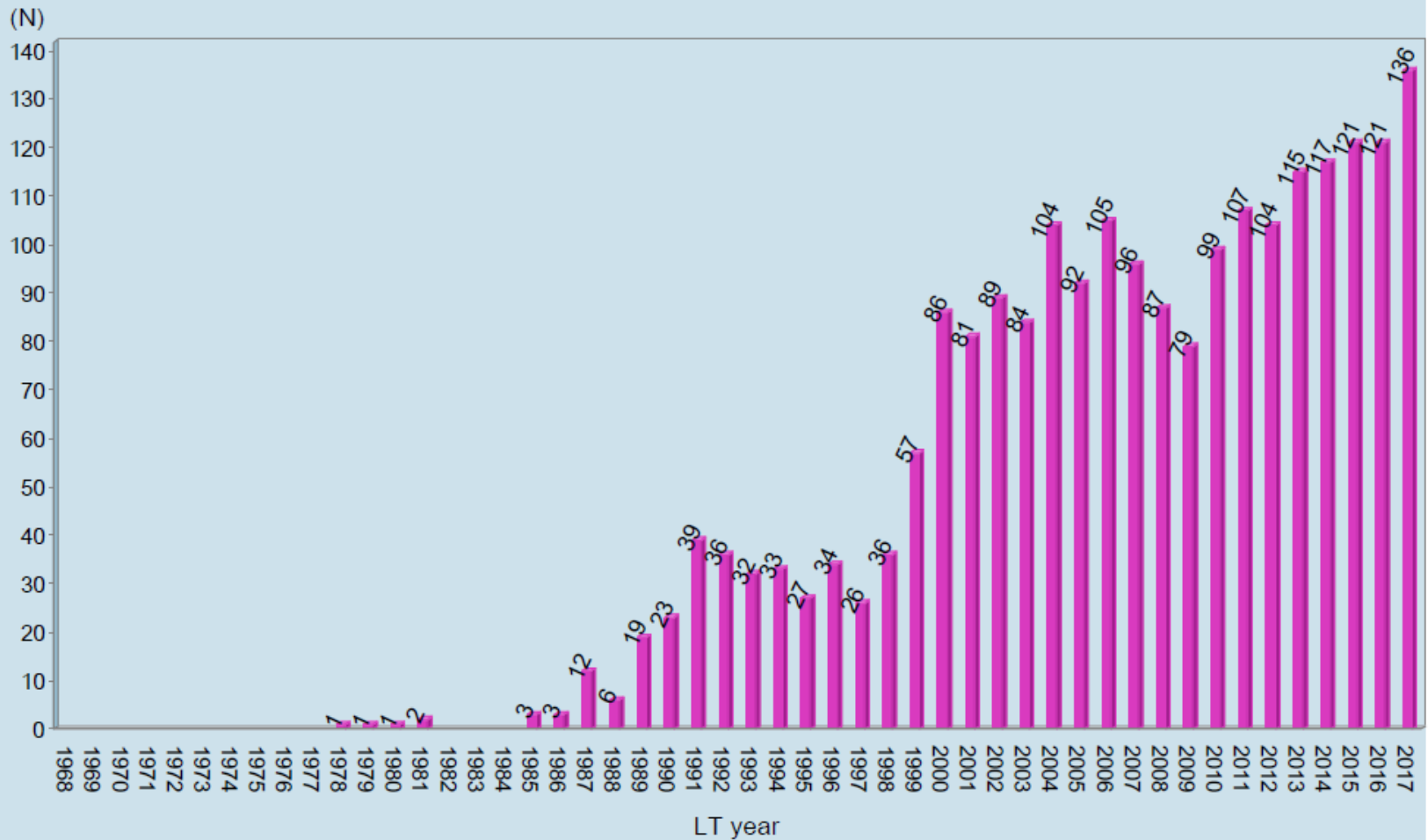
IL2



« Programmes de greffe »

FRRENN : Liver Transplantation Period

N = 2,214 Adults (1968-2017)



Une qualité de vie exceptionnelle

- 2 ou 3 comprimés chaque matin
- 1 à 2 visites par an
- Une vie sociale et professionnelle normale
- Grossesse possible **si arrêt MMF**



1990 – 2000

Exploration des limites

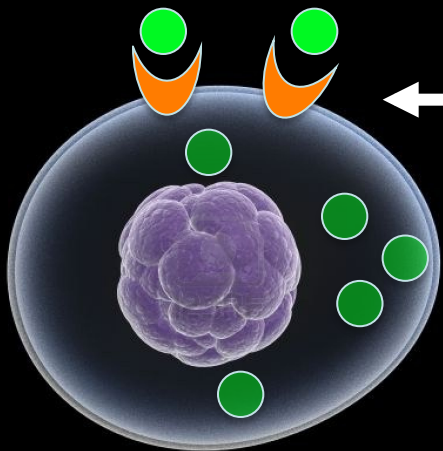
Développements techniques

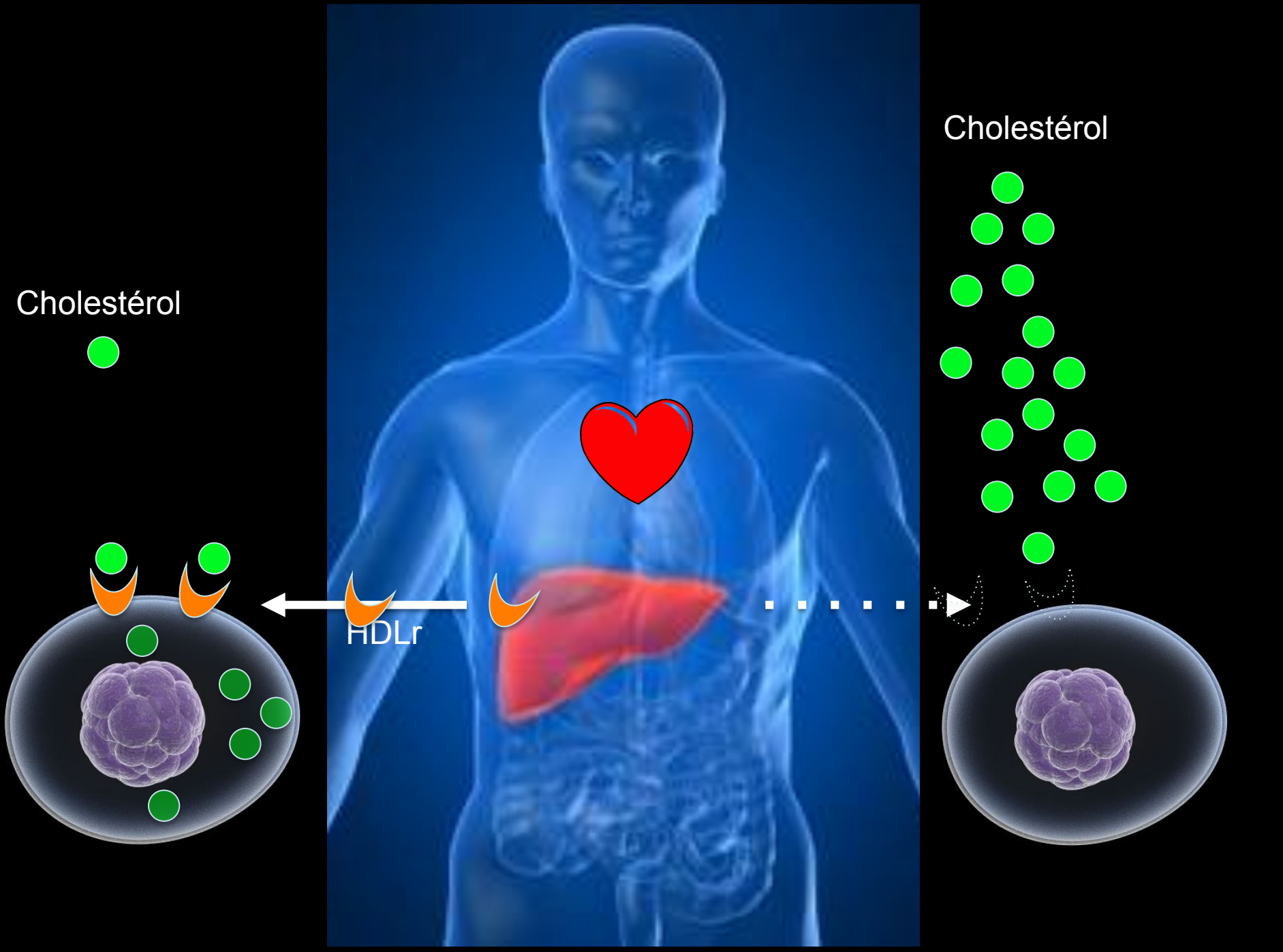


Cholestérol

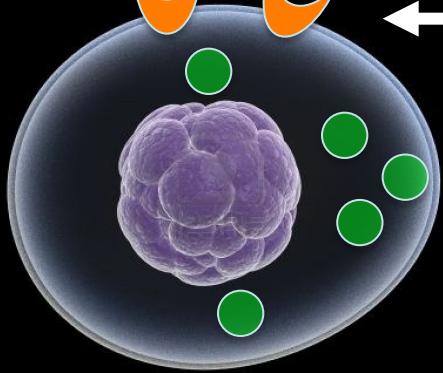


HDLr



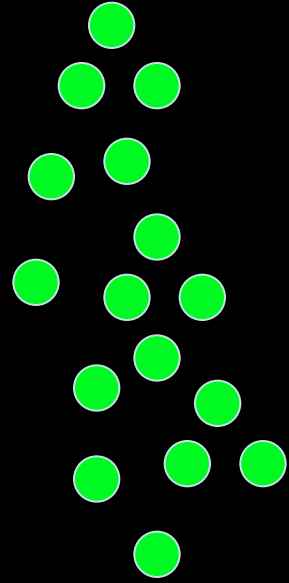


Cholestérol



HDLr

Cholestérol



Greffes multiples

- Cœur + poumon
- Cœur + rein
- Rein + pancréas
- Rein + foie + pancréas
- Cœur + poumons + foie + rein

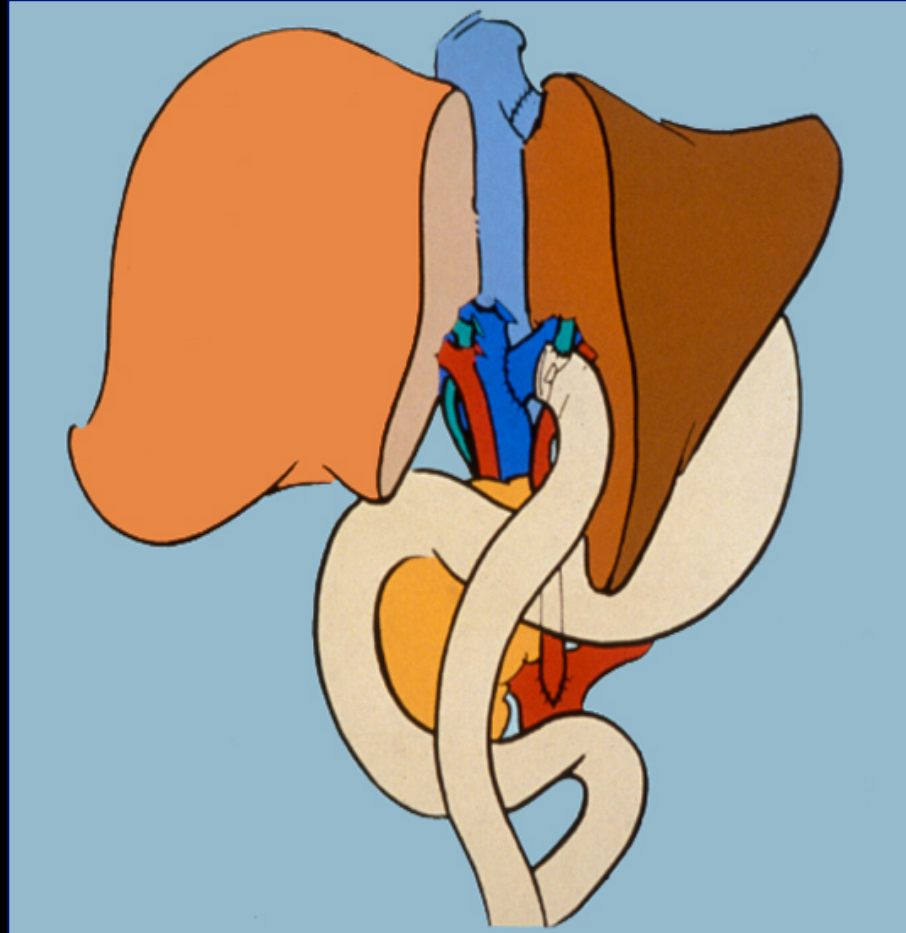
Jennifer 18 ans (Rennes-Nantes Août 2006)



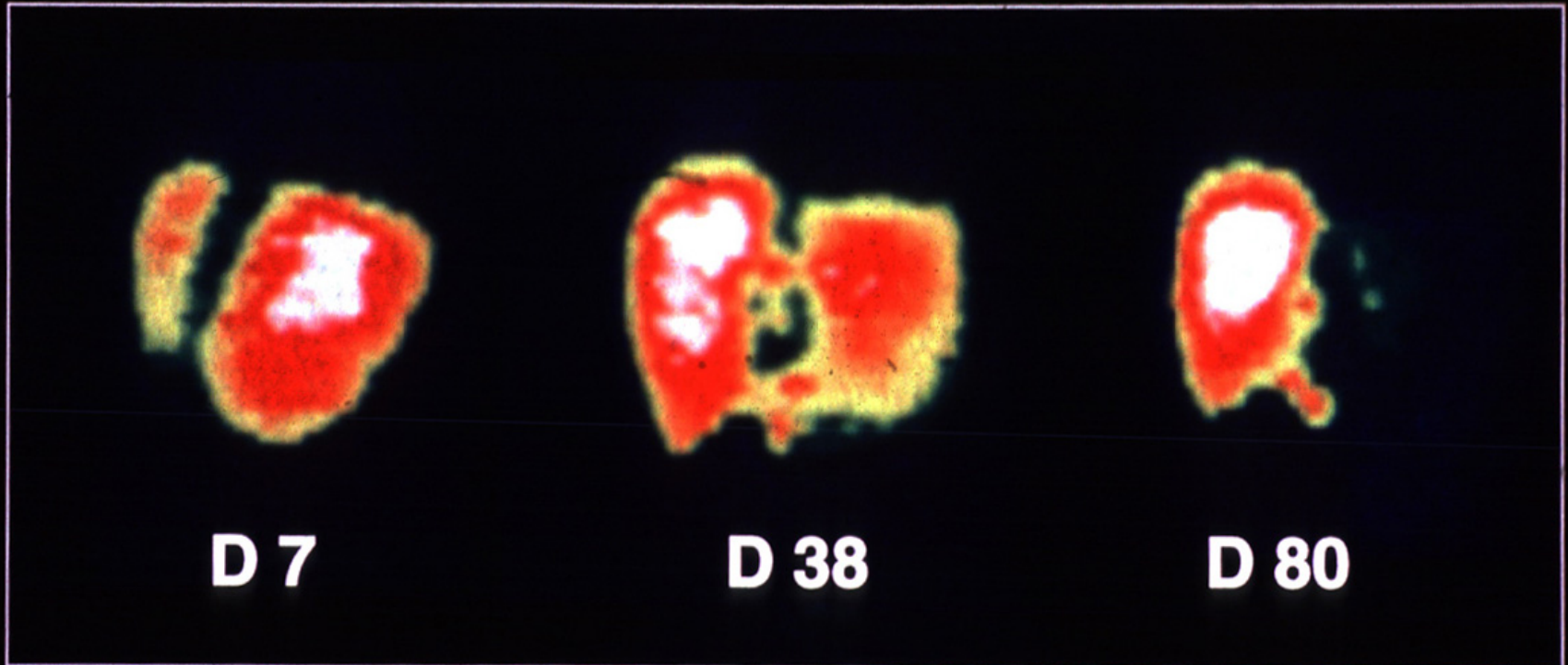
Greffes abdominales



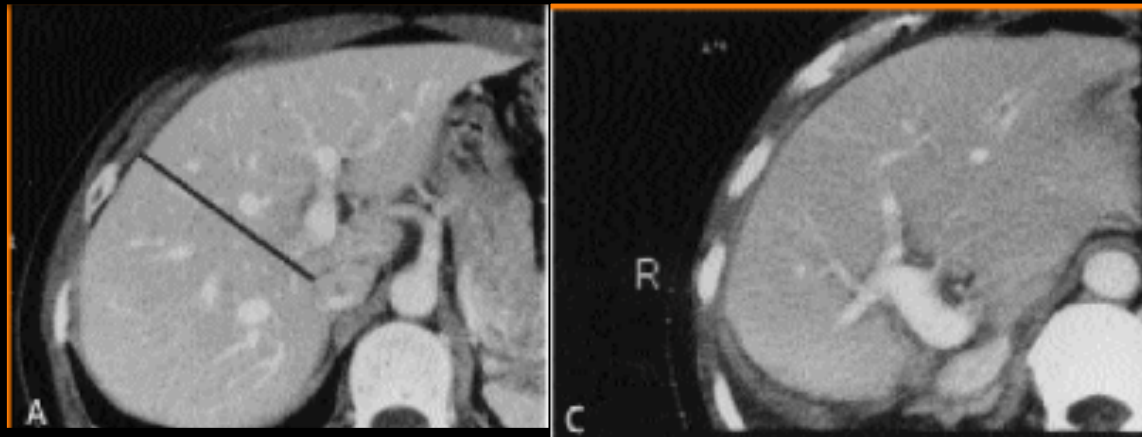
Greffes temporaires foie auxiliaire



ALT # 1



Greffes à donneur vivant





ALGER
Première greffe de foie; DVA
16 février 2003