

Tissue Typing by Skin Grafting During Metamorphosis of the Toad *Xenopus laevis* (Daudin)

During metamorphosis, the possibility of inducing an immunologically specific tolerance to skin allografts between individuals of the toad *Xenopus laevis* by skin grafts has been reported¹. This tolerance seems to be permanent². Sibling tolerance can be observed during a short period between stage 56 of NIEUWKOOP and FABER³ and 1 month after metamorphosis.

In the present study, we blocked *Xenopus laevis* siblings at metamorphosis in an attempt to lengthen the period in which tolerance can be induced. 31 stage 58 larvae were grown in 5×10^{-3} M. thiourea. This chemical is known to block the release of thyroxin by the thyroid gland. The blocked hosts received one, two or three 2 mm² skin grafts at a time from different untreated donor animals. The hosts received no other grafts until the fate of the first set of grafts was ascertained. Sometimes, a second and third set of grafts was then performed on the same hosts. Skin graft technique was the same as previously described².

The result of the block was that animals could tolerate grafts performed more than 3 months after they had been blocked. By this time untreated animals rejected 97% of the grafts². In the figure, the fate of the tested grafts is depicted: there are 4 classes for the donors and, corre-

sponding to them, 4 classes of hosts. 2 donors were placed in the same class if their skin could be accepted by the same set of animals, belonging to 1 class of hosts, and if their skin was rejected by animals of the other 3 classes of hosts. The hypothesis of 4 equivalent classes was verified with a probability between 20% and 30% of the cases.

From the present experiment, we may hypothesize that graft rejection capacity which is still detectable at metamorphosis, is controlled by one genetic region that is likely to correspond, as already suggested¹, to the major histocompatibility complex⁴. Furthermore, the fact that the period in which tolerance can be induced is prolonged by the thiourea treatment points out that thyroid hormone may play a major part in this tolerance phenomenon. Several facts indicate a direct action of thyroxin on lymphomyeloid organs of metamorphosing larvae. The thymus of *Rana pipiens* is heavily labelled after administration of ¹⁴C or ¹²⁵I labelled thyroxin⁵. In vitro, the regression of *Rana catesbeiana* lymph gland is obtained after supplying thyroxin to the culture medium⁶. Finally, a recent work⁷ suggests the existence of nuclear receptor sites in human lymphocytes which bind thyroxin.

In a preliminary experiment we grafted 8 thiourea-treated adult siblings and 8 untreated animals. The onset of rejection was slightly delayed for the treated animals (mean \pm S.D. was 12.0 ± 1.1 days for untreated animals and 14.2 ± 1.5 for thiourea treated ones). Rejection end point was also delayed for the treated toads (from 20.7 ± 3.6 to 22.7 ± 2.0). But the differences had no statistical significance. It seems that the effect of the block may be limited to the metamorphic period. Further study of the possible interaction between thyroid hormone and the immune response during metamorphosis, is necessary to exclude a non-immunological component in this system.

Résumé. Un traitement bloquant la métamorphose de *Xenopus laevis* a permis de prolonger la période où l'on peut induire la tolérance aux allogreffes de peau. Les animaux ont été groupés en quatre classes où les greffes sont histocompatibles et tolérées.

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		DONORS									
		1	2	3	4	1	2	3	4	1	2
		A	B	C	D	E	F	G	H	I	J
1	1	+									
	2	+									
	3	+									
	4	+									
	5	+									
	6	+									
	7	+									
	8	+									
2	9		+	+	+						
	10		+	+							
	11		+	+							
	12		+								
	13		+								
	14										
3	15						+	+	+		
	16						+	+	+		
	17						+	+	+		
	18						+	+	+		
	19						+	+	+		
	20						+	+	+		
	21									+	
	22						+	+	+		
	23						+	+	+		
	24									+	
	25						+	+	+		
	26										+
4	27										+
	28										+
	29										+
	30									+	+
	31									+	+

Donors and hosts are grouped in 4 classes according to results of the grafts. (+) means more than 10 days tolerated graft and (−) rejected graft.

¹ X. CHARDONNENS and L. DU PASQUIER, Eur. J. Immun. 3, 569 (1973).

² N. BERNARDINI, X. CHARDONNENS and D. SIMON, C. r. Acad. Sci., Paris D 269, 1011 (1969).

³ P. D. NIEUWKOOP and J. FABER, Normal Table of *Xenopus laevis* (Daudin) (North Holland Publishing Company, Amsterdam 1956).

⁴ L. DU PASQUIER, X. CHARDONNENS and V. C. MIGLIANO, Immunogenetics, in press.

⁵ A. REYNOLDS, in Hormones in Development (Eds. M. HAMBURGH and E. J. W. BARRINGTON; Appleton Century Crofts, New York 1971), p. 299.

⁶ H. B. RIVIÈRE and E. L. COOPER, Proc. Soc. exp. Biol. Med. 143, 320 (1973).

⁷ J. S. TSAI and H. H. SAMUELS, J. clin. Endocr. Metab. 38, 919 (1974).

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