
Эволюционная иммунология
Лекция 7 «Трансплантационный иммунитет»
Шилов Е.С.
26 марта 2018

Таблица 8.1.

Временные параметры и особенности отторжения алло(ксено)трансплантатов у животных различных типов

Тип, класс	Вид	Алло-, ксено-трансплантат	Время выживания, дни		Форма отторжения
			Первичный трансплантат	Вторичный трансплантат	
Губки	Ephydatia fluviatilis	Ал.	–	–	Образование коллагеноподобного слоя
	Axinella polypoides	Ал.	–	–	Образование зоны некроза
	Ephydatia fluviatilis, Eph. mulleri, Spongilla lacustris, Eunapius fragilis	Кс.	–	–	То же
	Hymeniacidon sinapium	Ал.	–	–	»
	Callispongia diffusa	Ал.	11,3	7,0	»
	Xestospongia exigus	Ал.	8,2	3,2	»
	Hymeniacidon perleve	Ал.	10,4	7,0	»
Кишечнополостные	Hydractinia echinata	Ал.	–	–	Гиперпластический рост
	Anthopleura elegantissima, Anth. krebsi, Leptogorgia vitgulata	Ал., Кс.	–	–	Гиперпластический рост или образование зоны некроза
	Eunicella stricta, Lophogorgia sarmentosa	Ал., Кс.	–	–	Образование зоны некроза
	Montipora verrucosa	Ал.	22,0	11,6	То же
Немертины	Lineus sanguineus → L. ruber	Кс.	15,4	8,6	Образование зоны некроза, депигментация ткани
	L. ruber → L. sanguineus	Кс.	16,4	8,6	То же
Членистоногие	Blamberus giganteus → Periplaneta americana	Кс.	>3	–	Инкапсуляция
Иглокожие	Cucumaria tricolor	Ал.	129–185	≈50	Образование зоны некроза, депигментация ткани
	Dermasterias imbricata	Ал.	–	–	То же
	Strongylocentrotus droebachiensis	Ал.	30	12	»
Оболочники	Styela plicata	Ал.	38	28	»

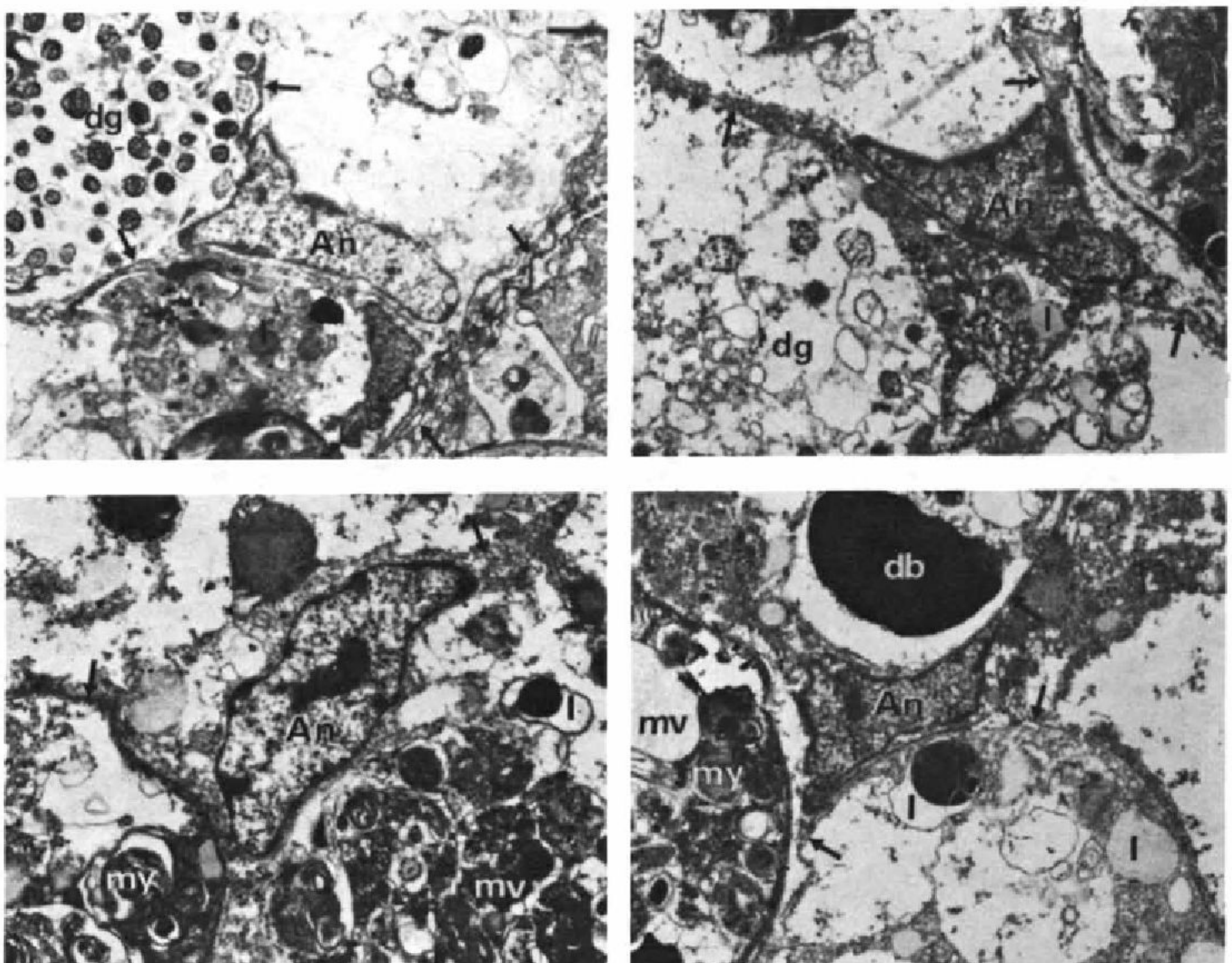
Table 1. Phyletic survey of chimera formation and somatic tissue compatibility*

Group	Mechanism of chimera formation	Evidence of somatic tissue compatibility system†
Protists:		
Dictyostelids	Coaggregation, mutation	Failure to coaggregate, separation during migration or culmination
Myxomycetes	Plasmodium fusion	Failure of plasmoidia to fuse
Fungi:		
Phycomycetes	Mutation	Failure of hyphal fusion
Ascomycetes	Hyphal fusion	
Basidiomycetes	Hyphal fusion	
Plants:		
Rhodophyta	Sporeling coalescence	Root fusion
Gymnosperms		
Angiosperms		
Animals:		
Porifera	Larval fusion	Failure of fusion, strain-specific reaggregation
Coelenterates	Planulae fusion	Failure to fuse
Annelids		Graft rejection
Molluscs		
Echinoderms		
Arthropods		Graft rejection
Chordates		
Ascidians	Colony fusion	Failure to fuse
Vertebrates	Bovine twins, malignancy	Lymphocyte-mediated immune response

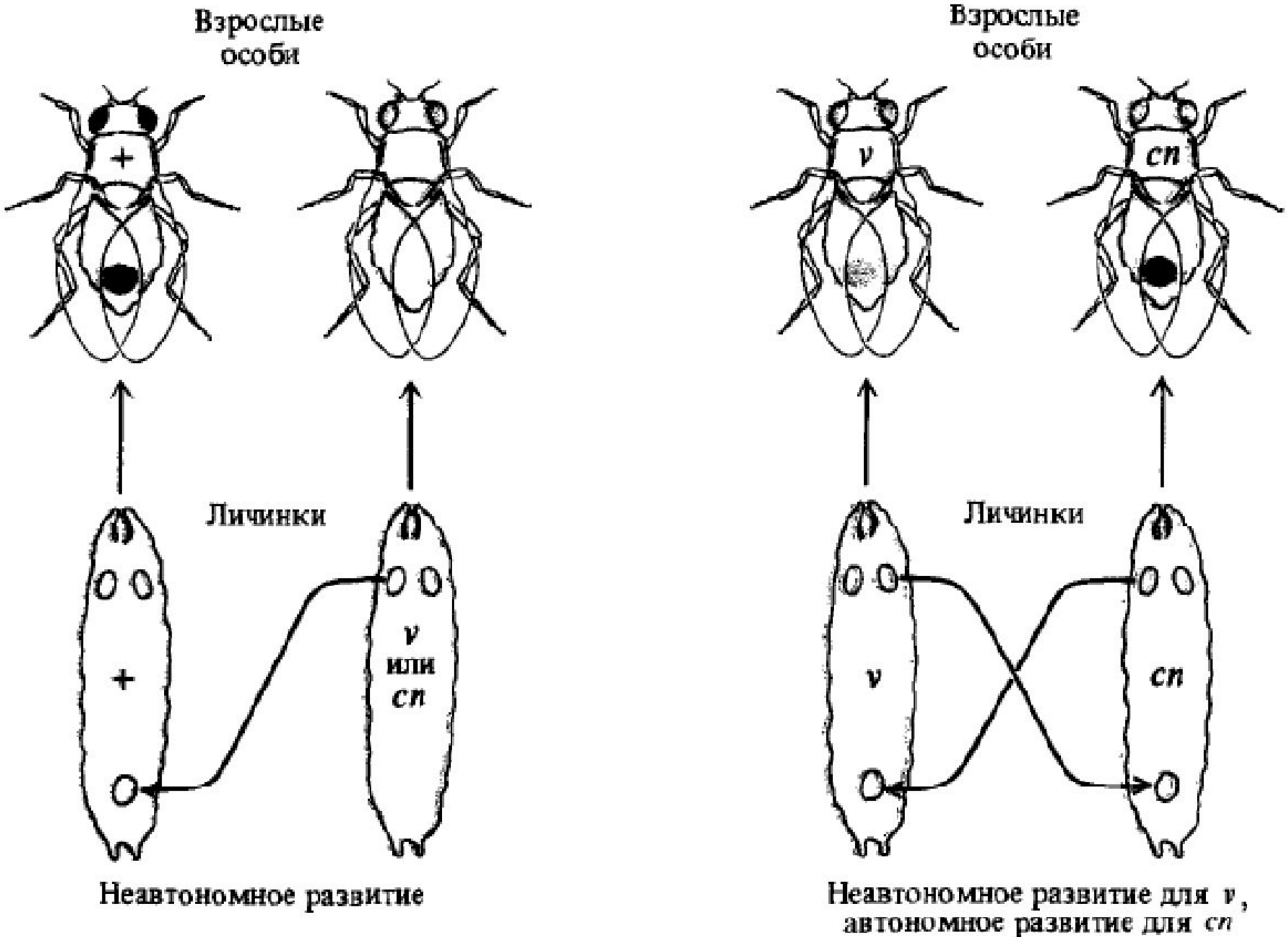
Table 1: Invertebrates exhibiting induction, specificity, and/or immunological memory in the nonpathogenic context of first and second challenges with transplants (n.a.: not analyzed).

Species	Challenge	Specifity	Memory	References
Porifera				
C. diffusa	Tissue (allograft) transplantation	+	+	Smith and Hildemann, 1986 [35]
G. cydonium		+	n.a.	Müller et al., 1999 [36]
Cnidaria				
E. stricta	Colonial contact/allograft, xenograft	+	n.a.	Theodor, 1970 [37]
M. verrucosa		+	+	Hildemann et al., 1977 [38]
Nemertea				
L. ruber *L. lacteus*	Tissue (allograft, xenograft) transplantation	+	+	Bierne and Langlet, 1974 [39]; Langlet and Bierne, 1975 [40]; 1982 [41]; 1984 [42]
Annelida				
Earthworms *L. terrestris E. fetida*	Tissue (allograft, xenograft) transplantation	+	+	Cooper, 1969 [43]; Cooper and Roch, 1986 [44]
Leeches *H. medicinalis G. complanata*	Tissue (allograft, xenograft) transplantation	+	+	Tettamanti et al., 2003 [45]
Mollusca				
I. fruhstorferi	Tissue (allograft) Transplantation	+	n.a.	Yamaguchi et al., 1999 [46]
Arthropoda				
P. americana B. orientalis	Tissue (allograft, xenograft) transplantation	+	+	Hartmann and Karp, 1989 [47]; Karp and Meade, 1993 [48]
Echinodermata				
S. purpuratus L. pictus	Tissue (allograft) transplantation	+	−	Coffaro and Hinegardner, 1977 [49]
D. imbricata		+	+	Karp and Hildemann, 1976 [50]
Tunicata				
B. schlosseri	Colonial contact/allograft	+	n.a.	Rinkevich et al., 1998 [51]; Scofield et al., 1982 [52];
S. plicata		+	+	Raftos et al., 1987 [53]; 1988 [54]

Амебоциты инфильтрировались в аллотрансплантант немертины



Пересадка имагинальных дисков дрозофилы



Факторы агрегации губок

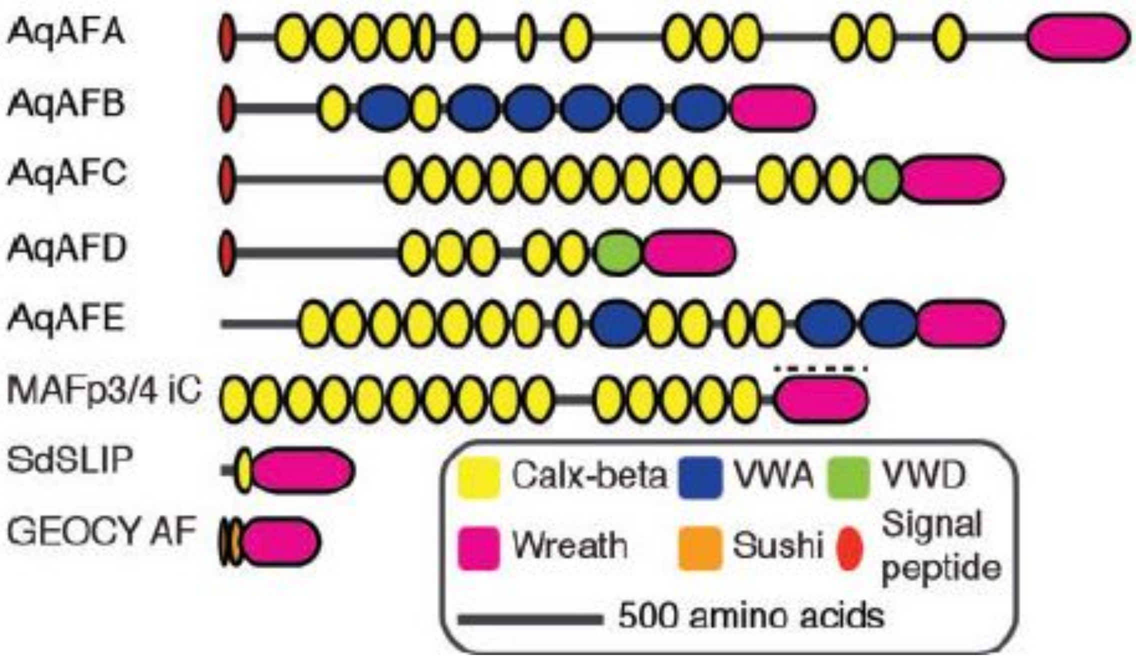
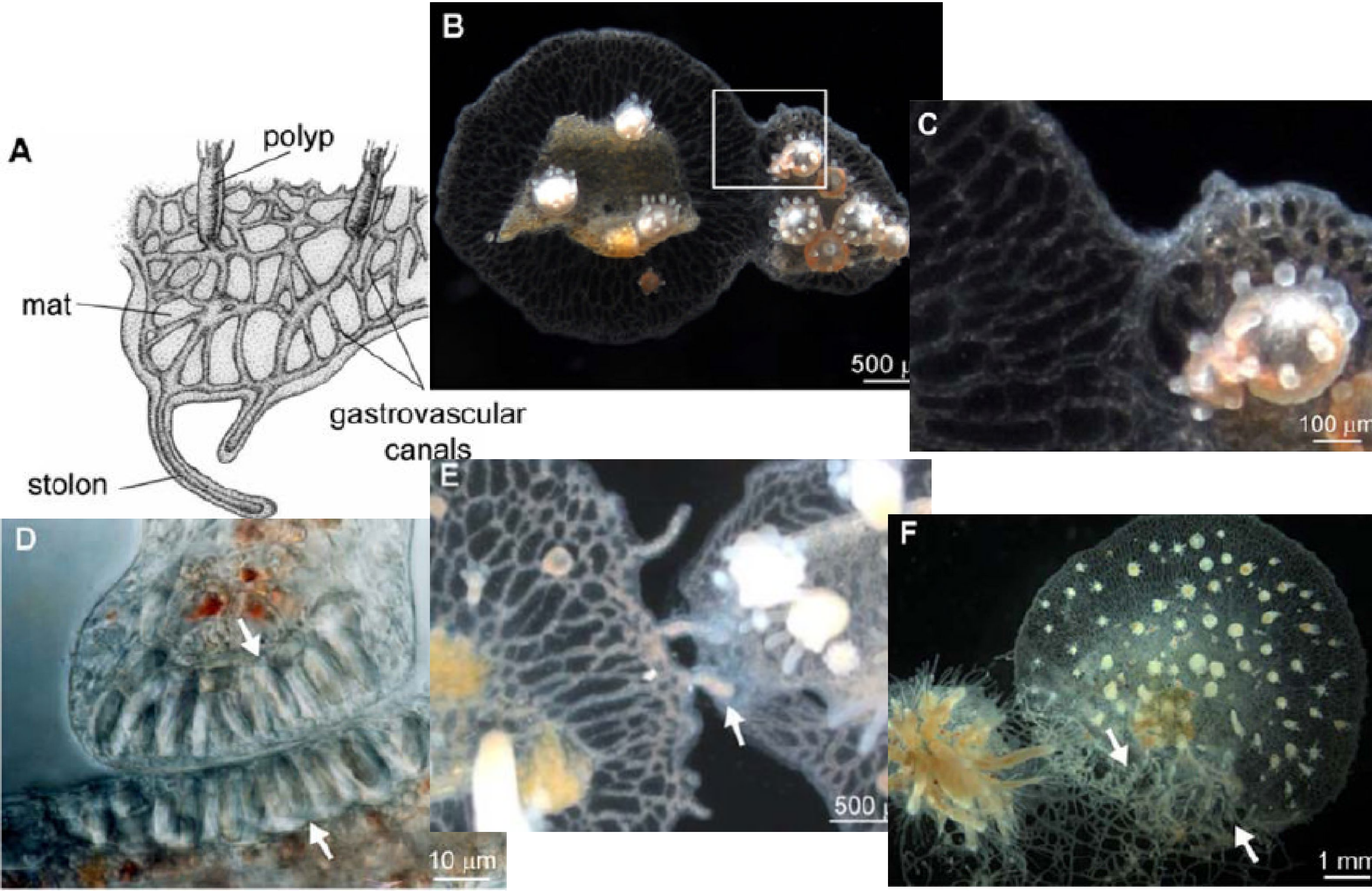


FIG. 1. Domain architecture of aggregation factor proteins. Aggregation factor proteins from *Amphimedon queenslandica* (AqAFA–AqAFE), *Clathria prolifera* (MAFp3/4 iC), *Suberites domuncula* (SdSLIP) and *Geodia cydonium* (GEOCY AF) are shown. Colored shapes represent predicted protein domains and sequence features. Models are approximately to scale. For *C. prolifera*, MAFp3 (indicated by dashed line) and MAFp4 are represented as a single contiguous sequence; the longest isoform (isoform C) is shown. iC, isoform C; VWA, von Willebrand type A domain; VWD, von Willebrand type D domain.

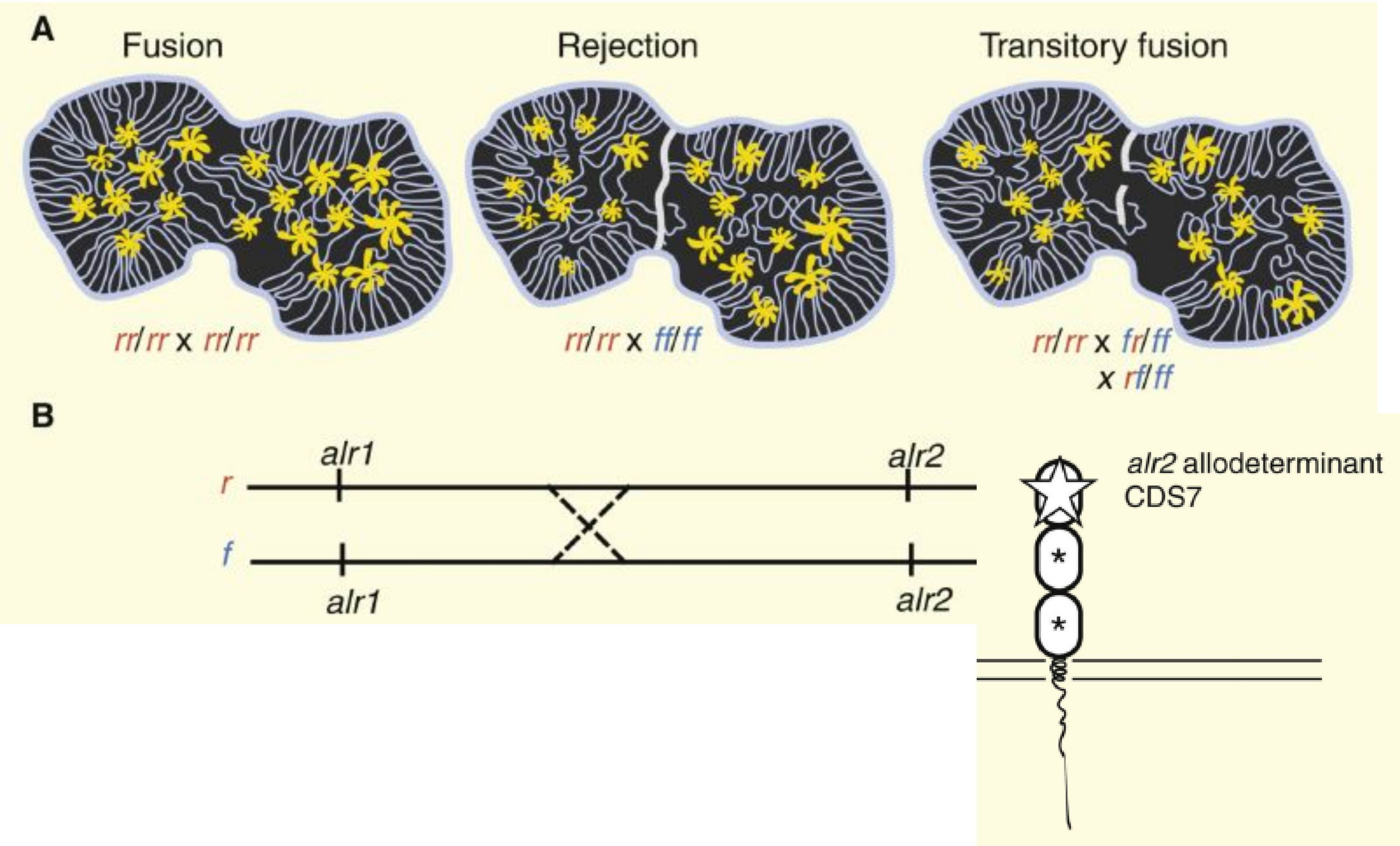
Amphimedon sp.

Clathria sp.

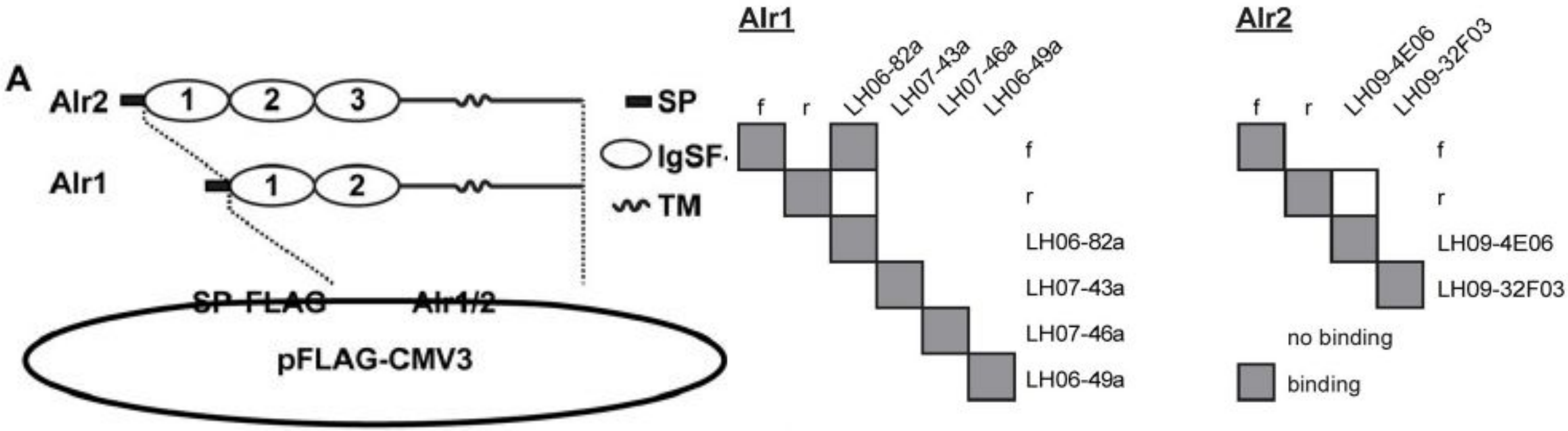
Слияние (верхний ряд) и отторжение (нижний) колоний у Hydractinia

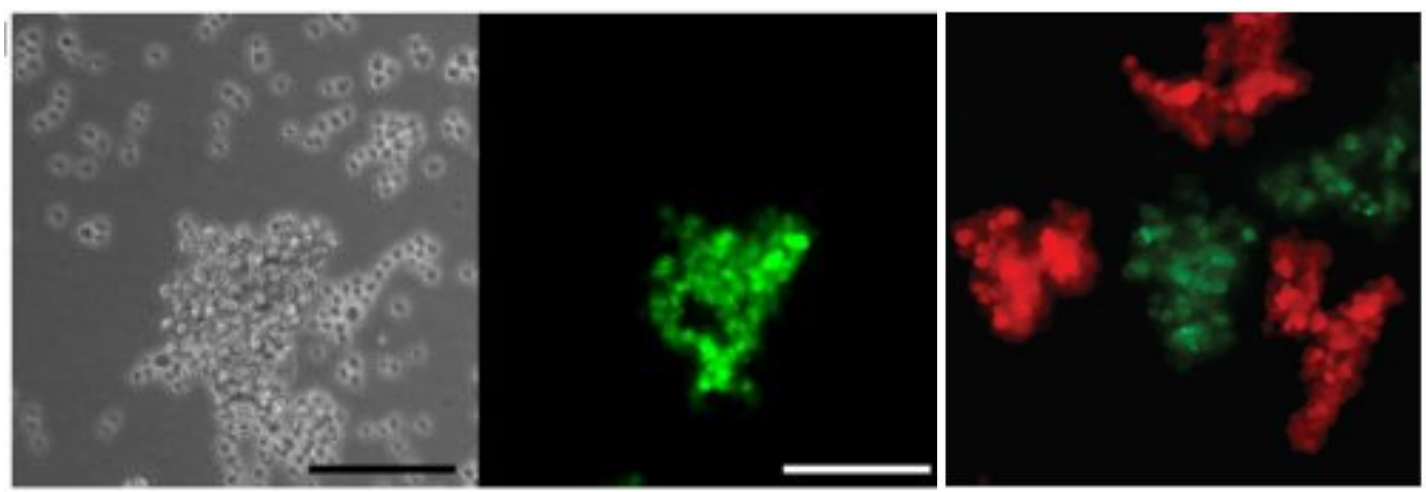


Отторжение чужих колоний у гидроида Hydractinia можно объяснить системой всего двух локусов, *alr1* и *alr2*



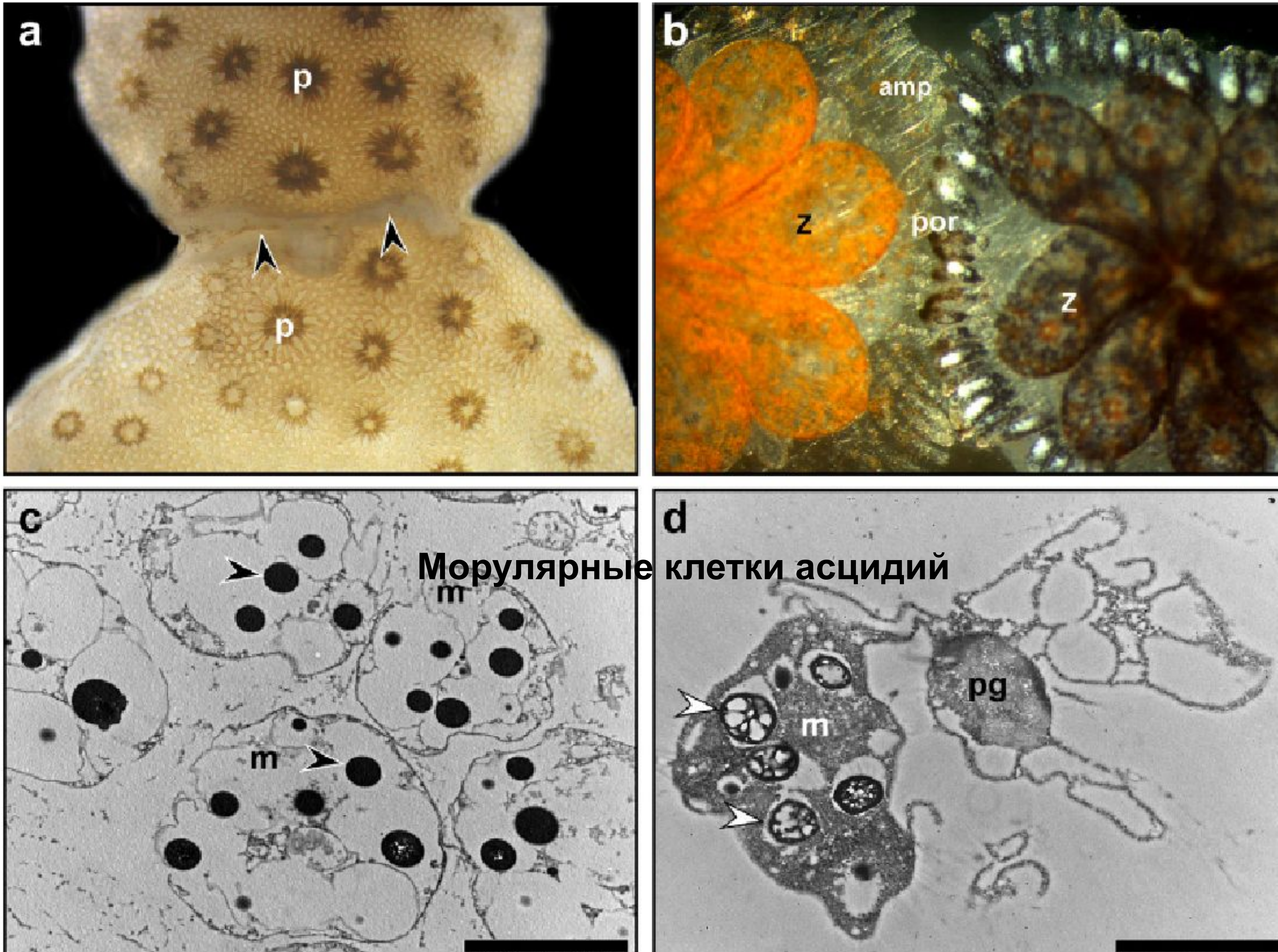
Гомофильное связывание изоформ Alr1 и Alr2 обеспечивает сегрегацию клеток





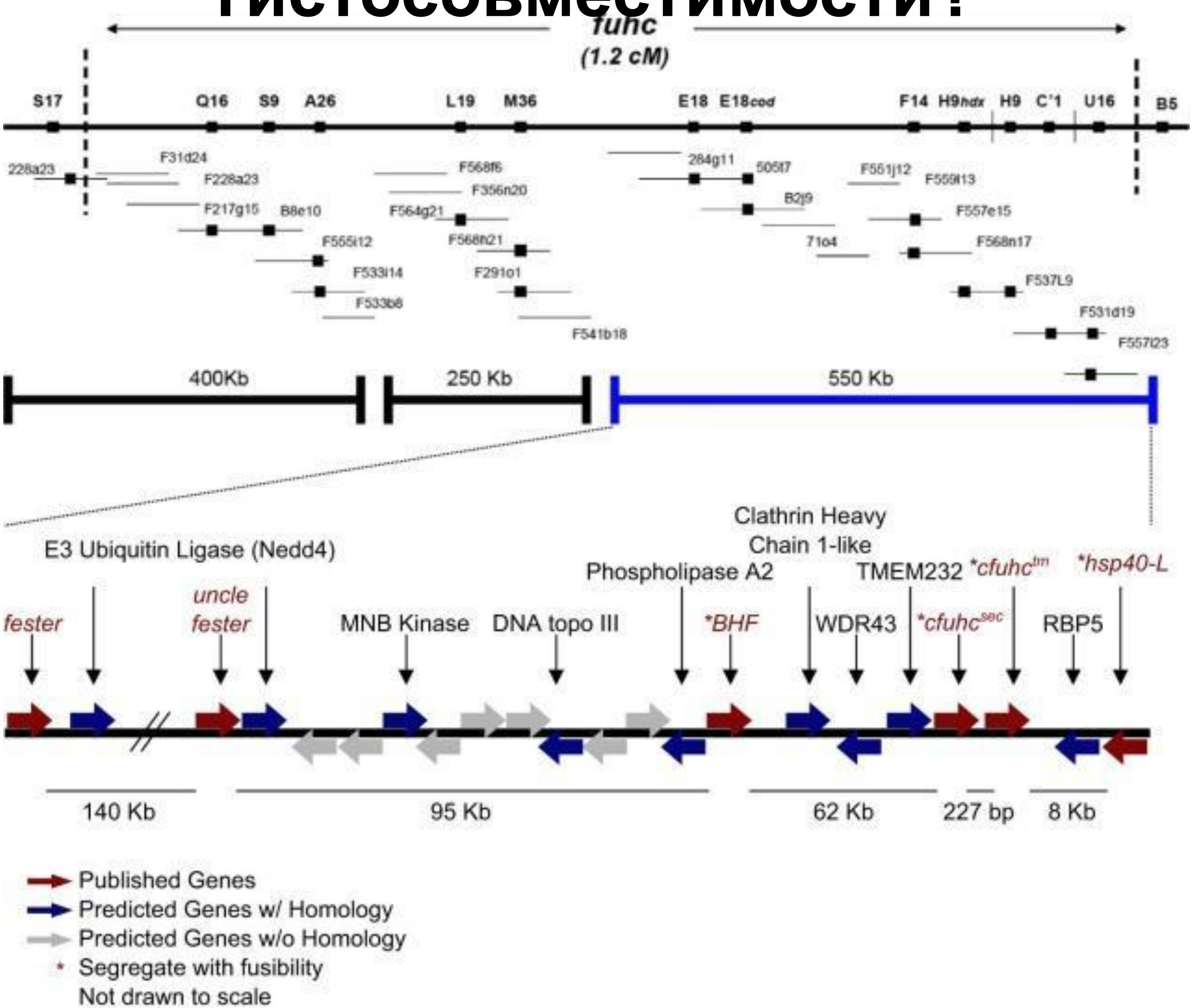
Агрегаты клеток CHO, трансфецированных флуоресцентным маркером и специфической изоформой Alr1

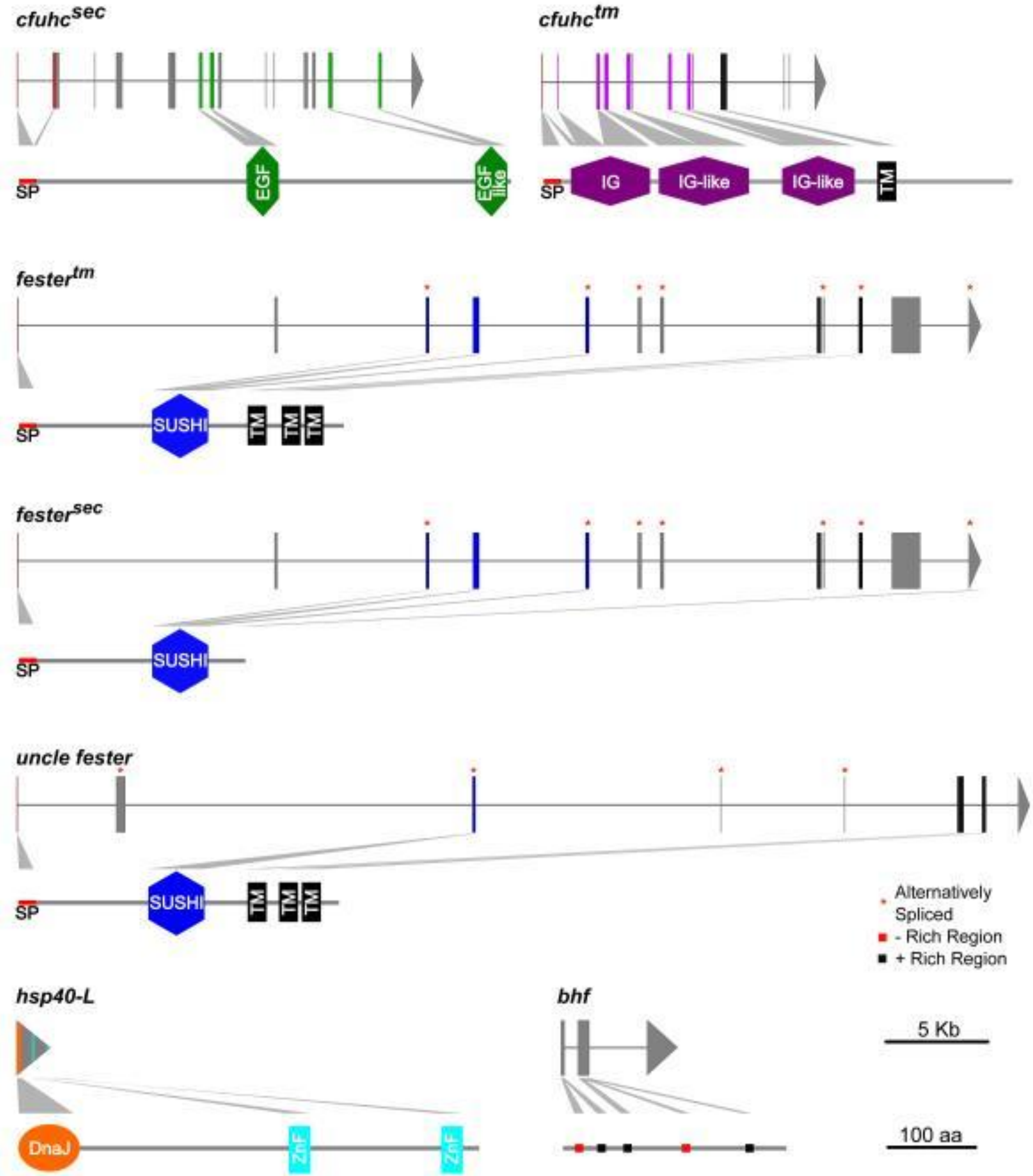
Полип Stylophora и асцидия Botryllus



Морулярные клетки асцидий

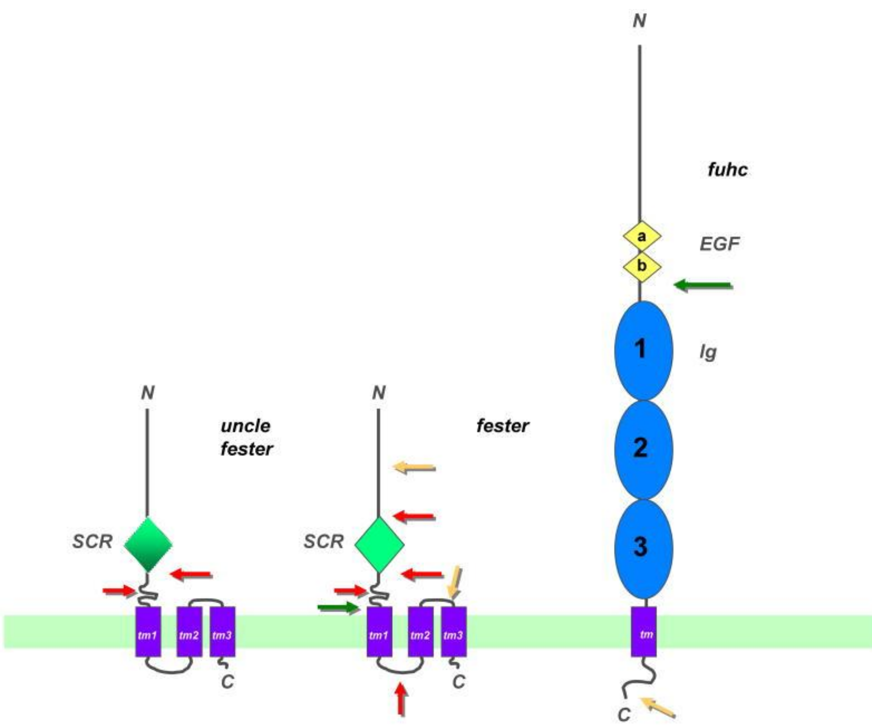
Локус *fuhc* асцидий содержит 6 генов гистосовместимости?

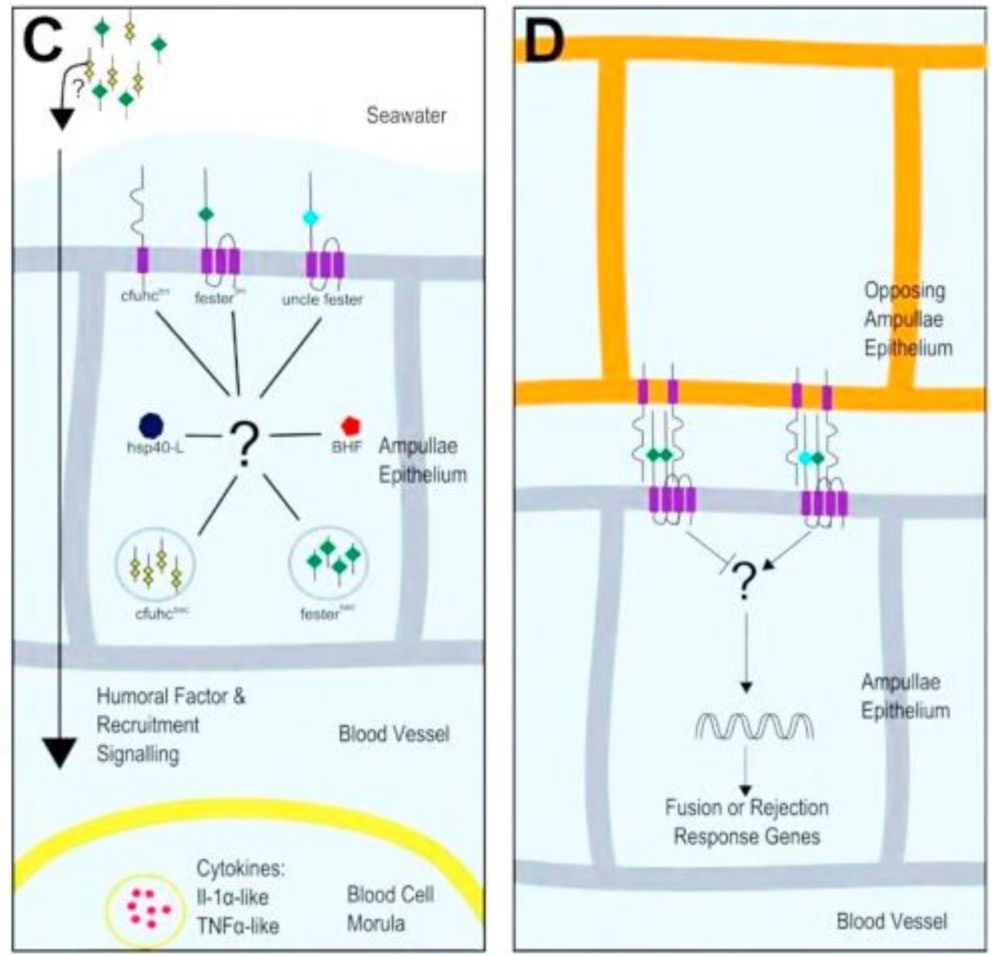




cfuhc^sec
SP
EGF
EGF like
cfuhc^tm
SP
IG
IG-like
IG-like
TM
fester^tm
SP
SUSHI
TM
TM
TM
fester^sec
SP
SUSHI
uncle fester
SP
SUSHI
TM
TM
TM
Alternatively Spliced
- Rich Region
+ Rich Region
hsp40-L
DnaJ
ZnF
ZnF
bhf
5 Kb
100 aa

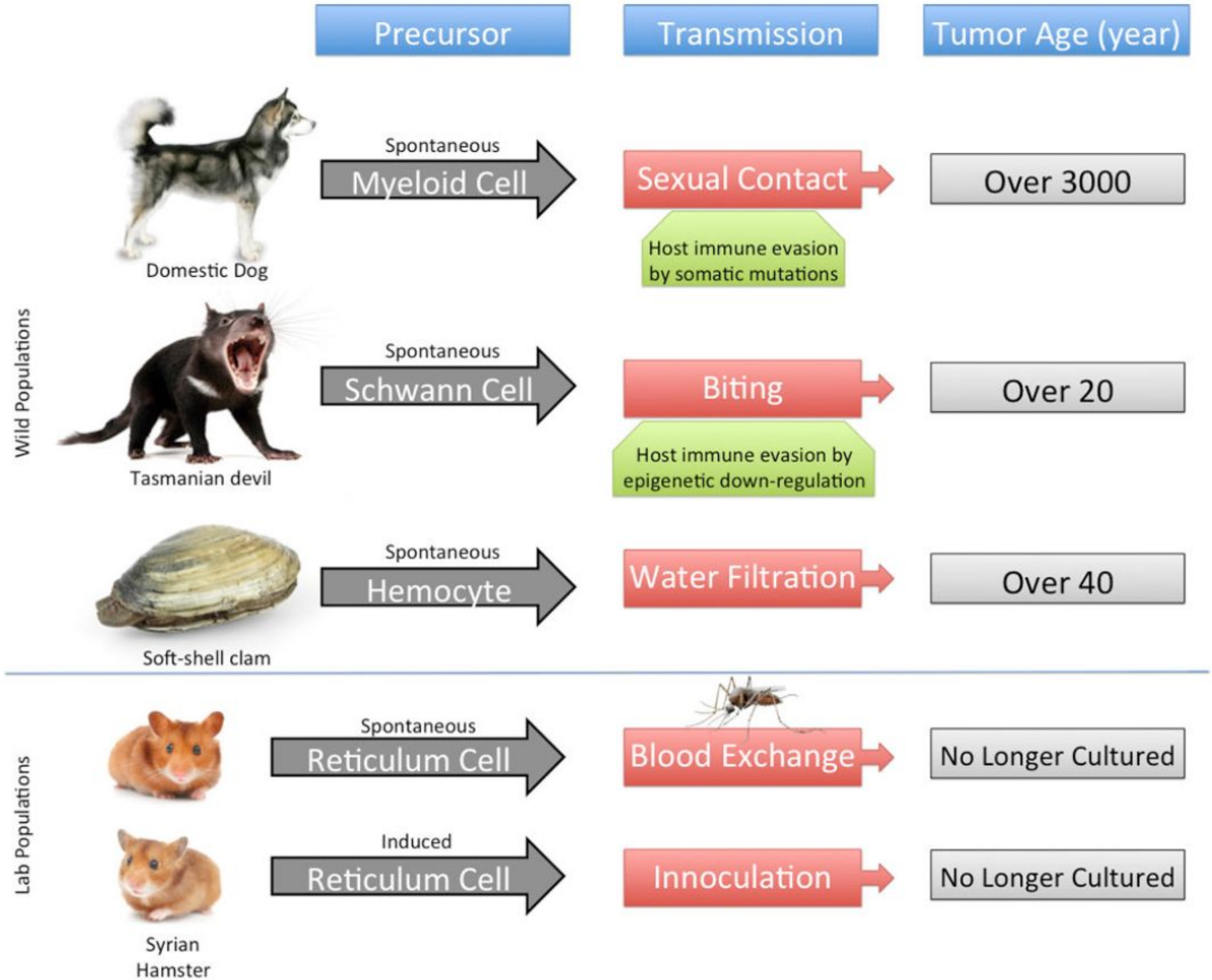
Адгезионные молекулы асцидий



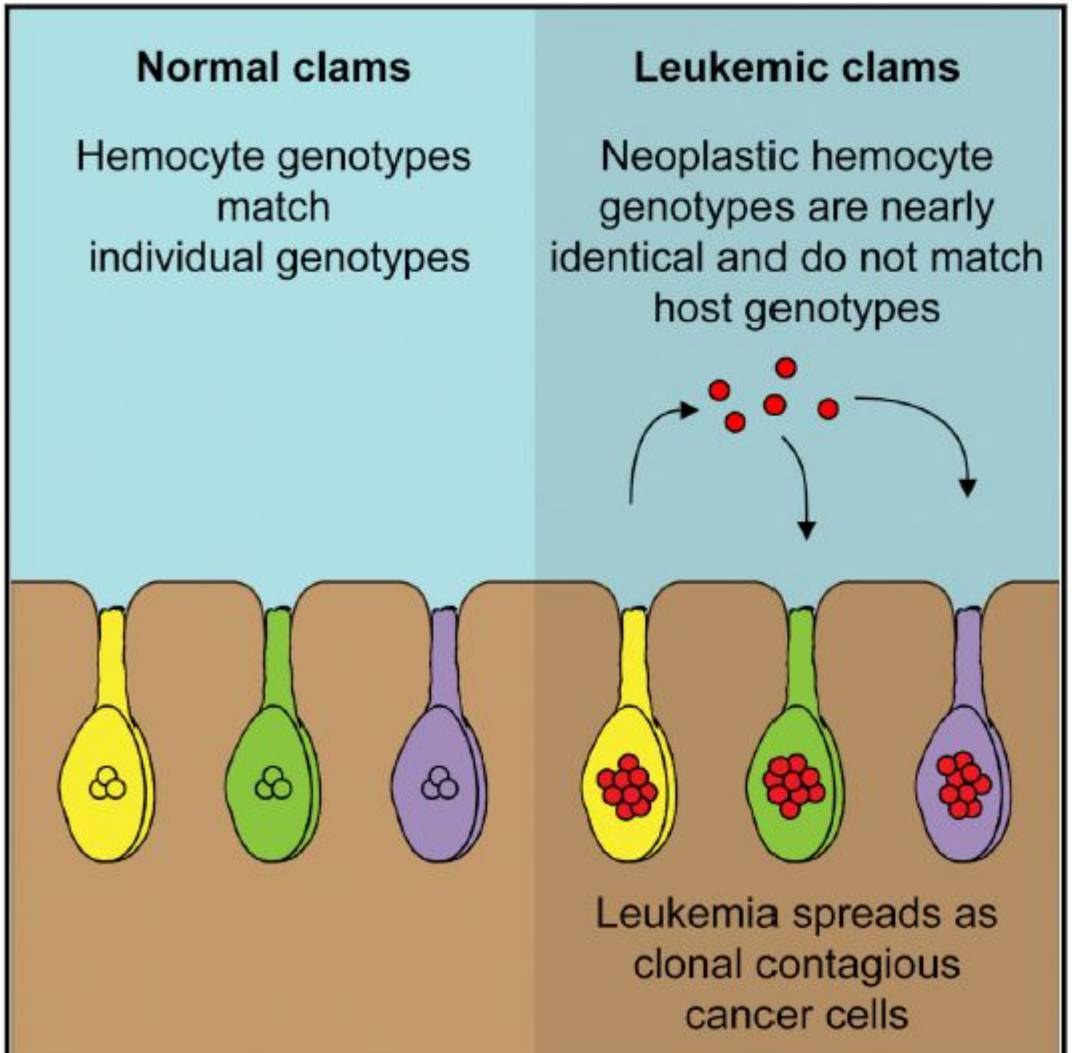


Uncle fester **fester** **cfuhc**

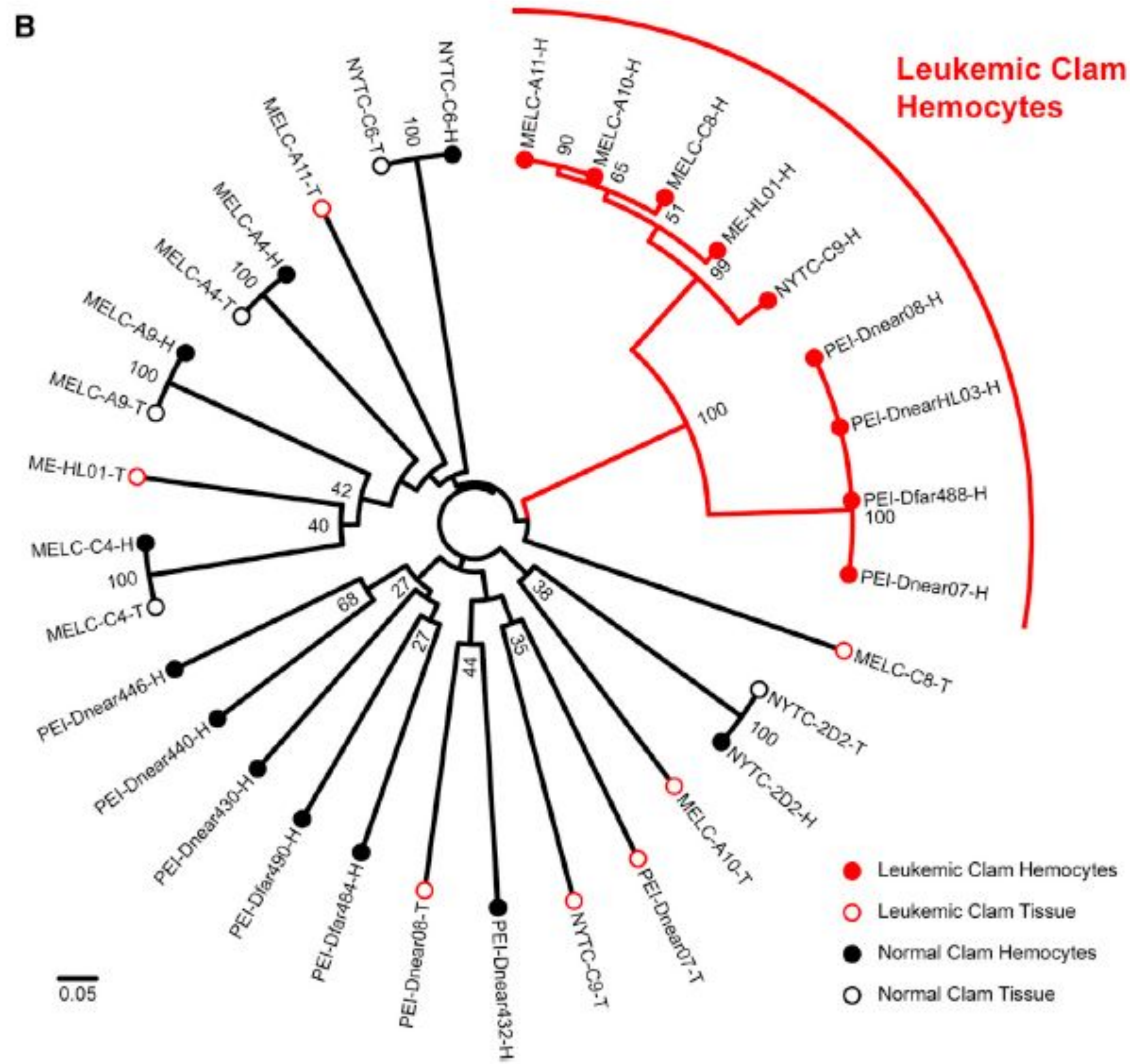
Трансмиссибельные опухоли



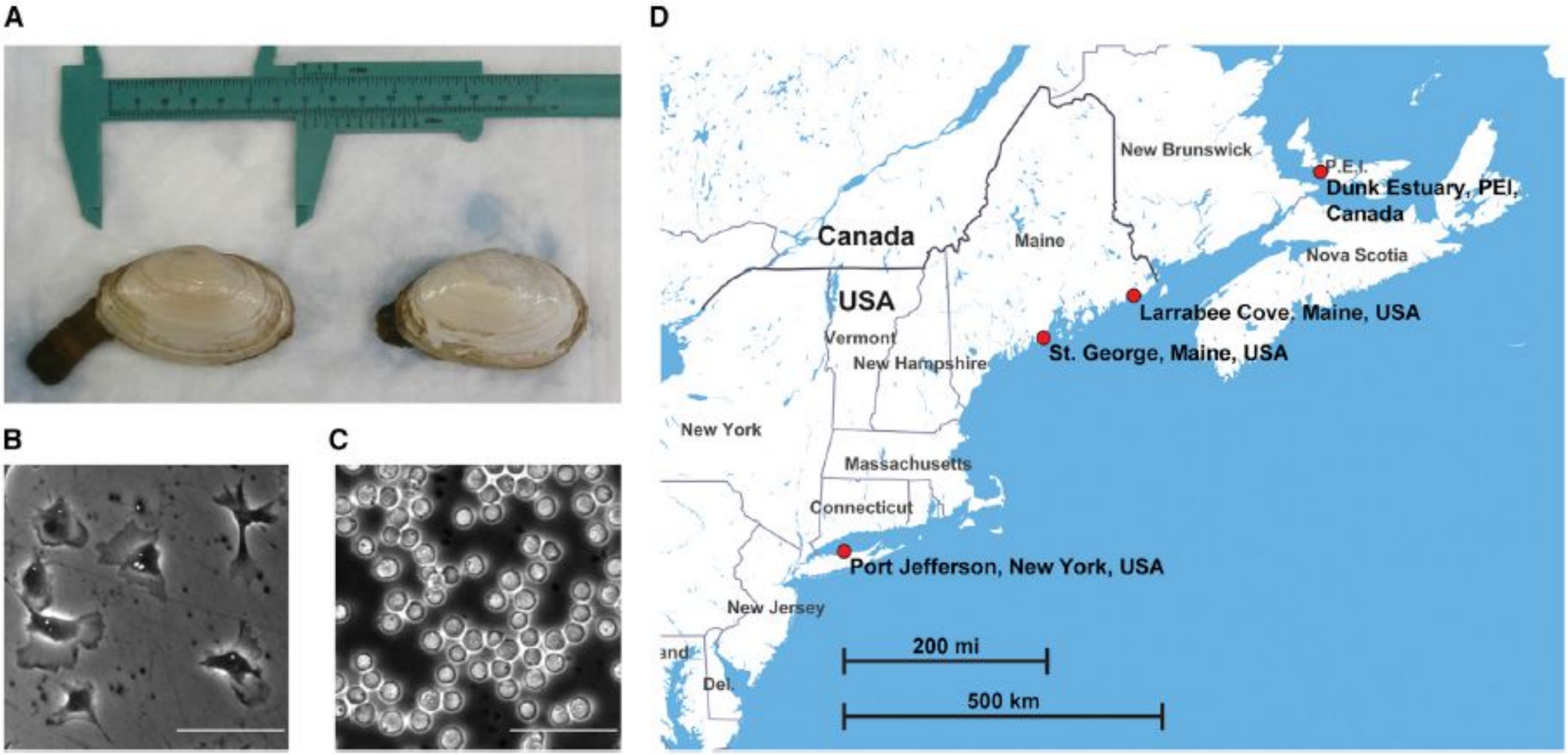
Лейкемия моллюсков *Mya arenaria*



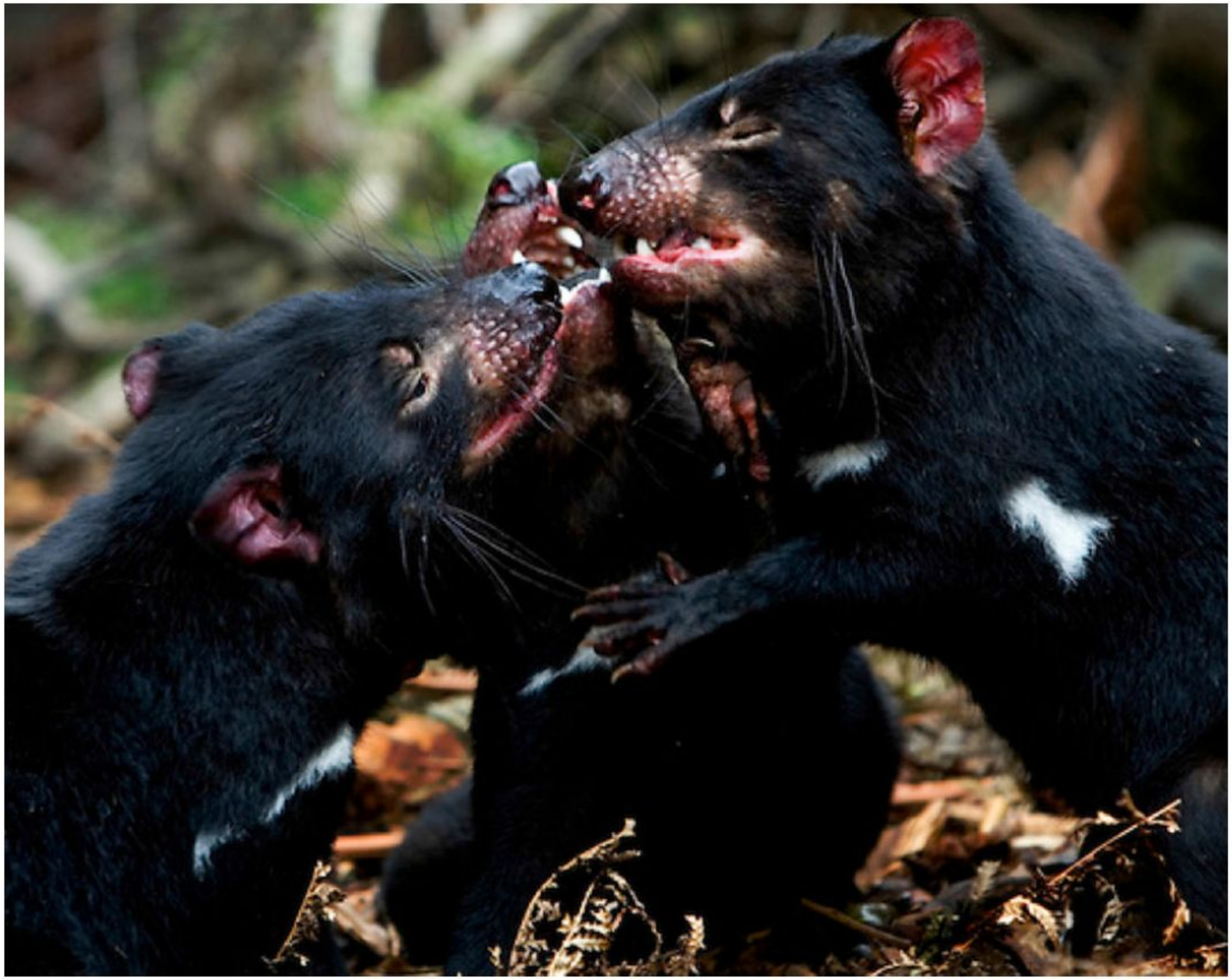
Опухолевые клетки имеют множественные копии транспозона Steamer и демонстрируют общее происхождение



Гольфстрим разносит опухолевые клетки моллюсков по мировому океану?

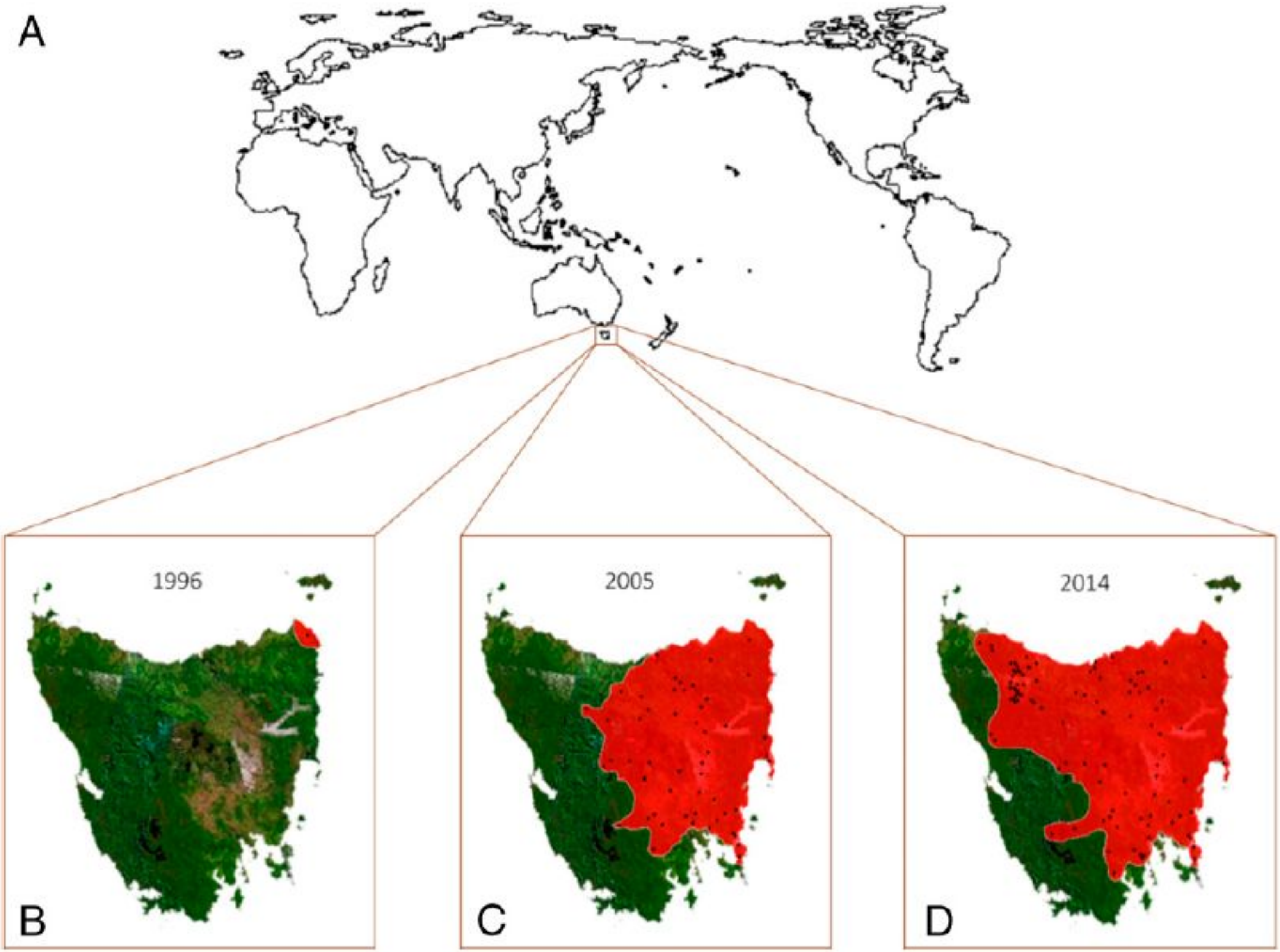


DFTD - Devil Facial Tumour Disease

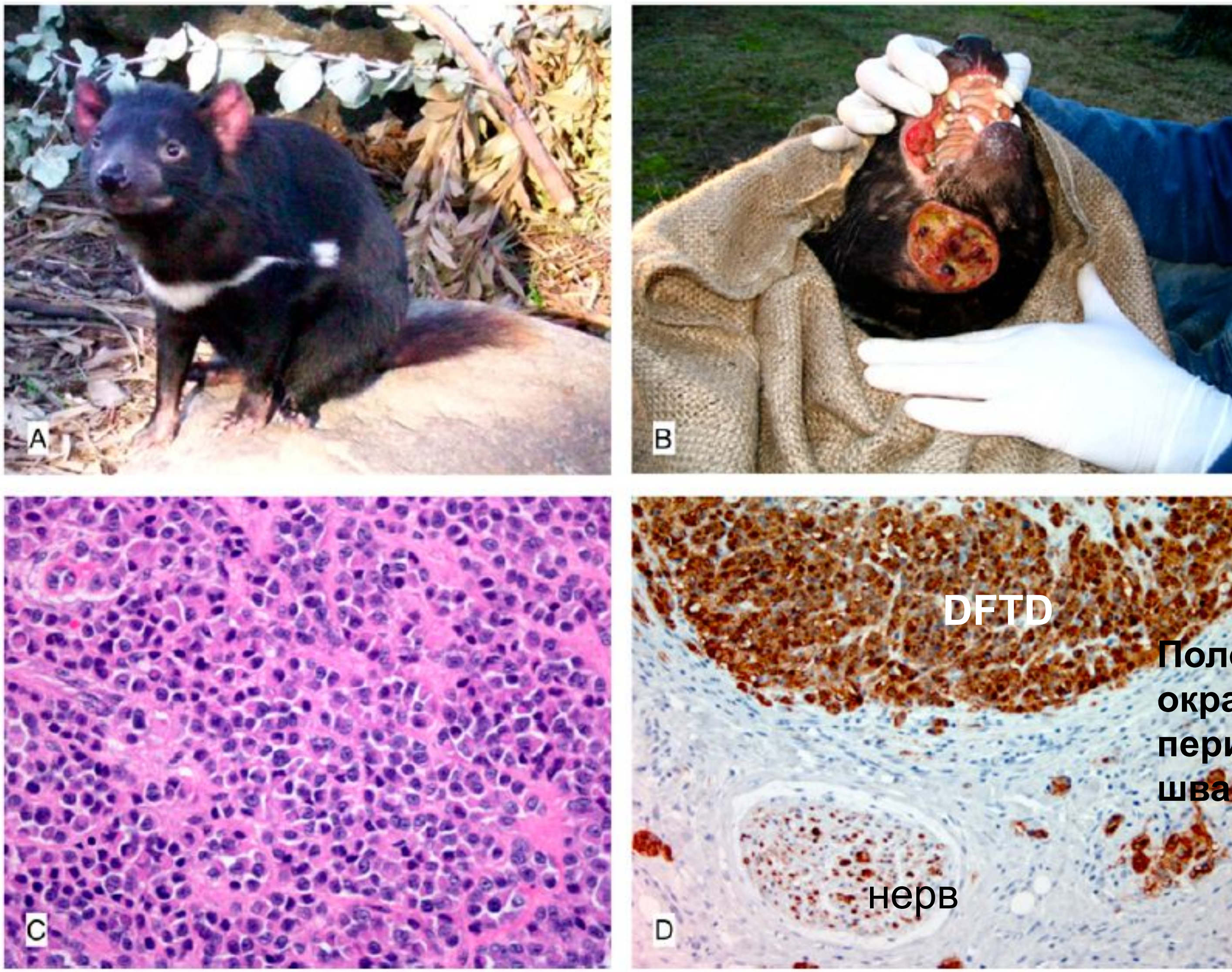


Высокоагрессивная опухоль, возникшая на основе Шванновской клетки, впервые описана в 1996 году, передается при укусах.

Распространение DFTD

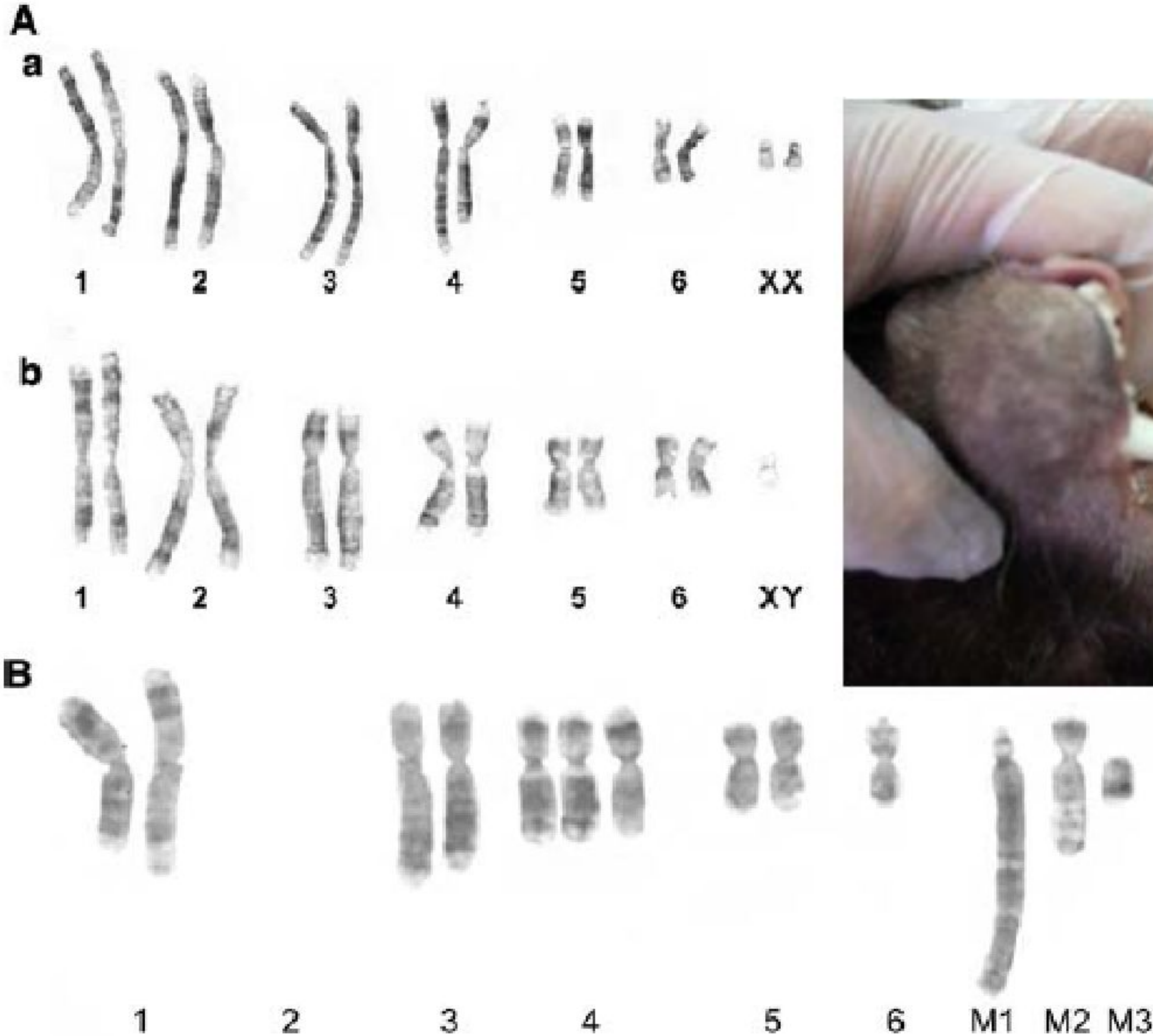


Происхождение DFTD доказывается с помощью иммуногистохимии



Положительное окрашивание на периаксин - белок шванновских клеток

Клональность DFTD



Таманские дьяволы действительно высоко изогенны по генам МНС

Table 3. MHC genotyping of Tasmanian devils used for skin graft experiments.

Tasmanian devil ID	MHC I $\alpha1$ sequence variants	MHC II $\beta1$ sequence variants
TD 190	Sahal*27, 28, 32, 35, 49	SahaDAB*01, 03, 05
TD 199	Sahal*27, 28, 32, 35, 49	SahaDAB*01, 03, 05
TD 187	Sahal*28, 32, 35, 49, 57	SahaDAB*01, 03, 05, 12
TD 200	Sahal*27, 28, 32, 35, 49	SahaDAB*01, 03, 05, 11
TD 188	Sahal*27, 32, 35, 49	SahaDAB*01, 03, 05, 15
TD 189	Sahal*27, 32, 35, 48	SahaDAB*01, 03, 05, 11, 15
TD 191	Sahal*28, 32, 34, 48, 49	SahaDAB*01, 03, 05, 13

TD 190 and TD 199 shared all MHC I and II alleles. The remaining devil pairs had two to three MHC I allelic mismatches and one to two MHC II allelic mismatches.
doi:10.1371/journal.pone.0022402.t003

Table 4. Amino acid difference count at peptide binding sites and MLR results within skin graft devil pairs.

Tasmanian devil ID	Amino acid difference count at peptide binding sites at MHC I $\alpha1$	Amino acid difference count at peptide binding sites at MHC II $\beta1$	Mixed lymphocyte reaction (SI)
TD 190 and TD 199	0	0	1
TD 187 and TD 200	0	0	1
TD 188 and TD 189	2	0	17
TD 190 and TD 191	0	0	5

TD 188 and TD 189 had two amino acid differences at peptide binding sites at MHC I $\alpha1$ and had a strong MLR response. The other three pairs did not have amino acid difference count at peptide binding sites at MHC I $\alpha1$ or MHC II $\beta1$ and had low MLR responses.
doi:10.1371/journal.pone.0022402.t004

Разницы генотипов между больными и здоровыми дьяволами нет

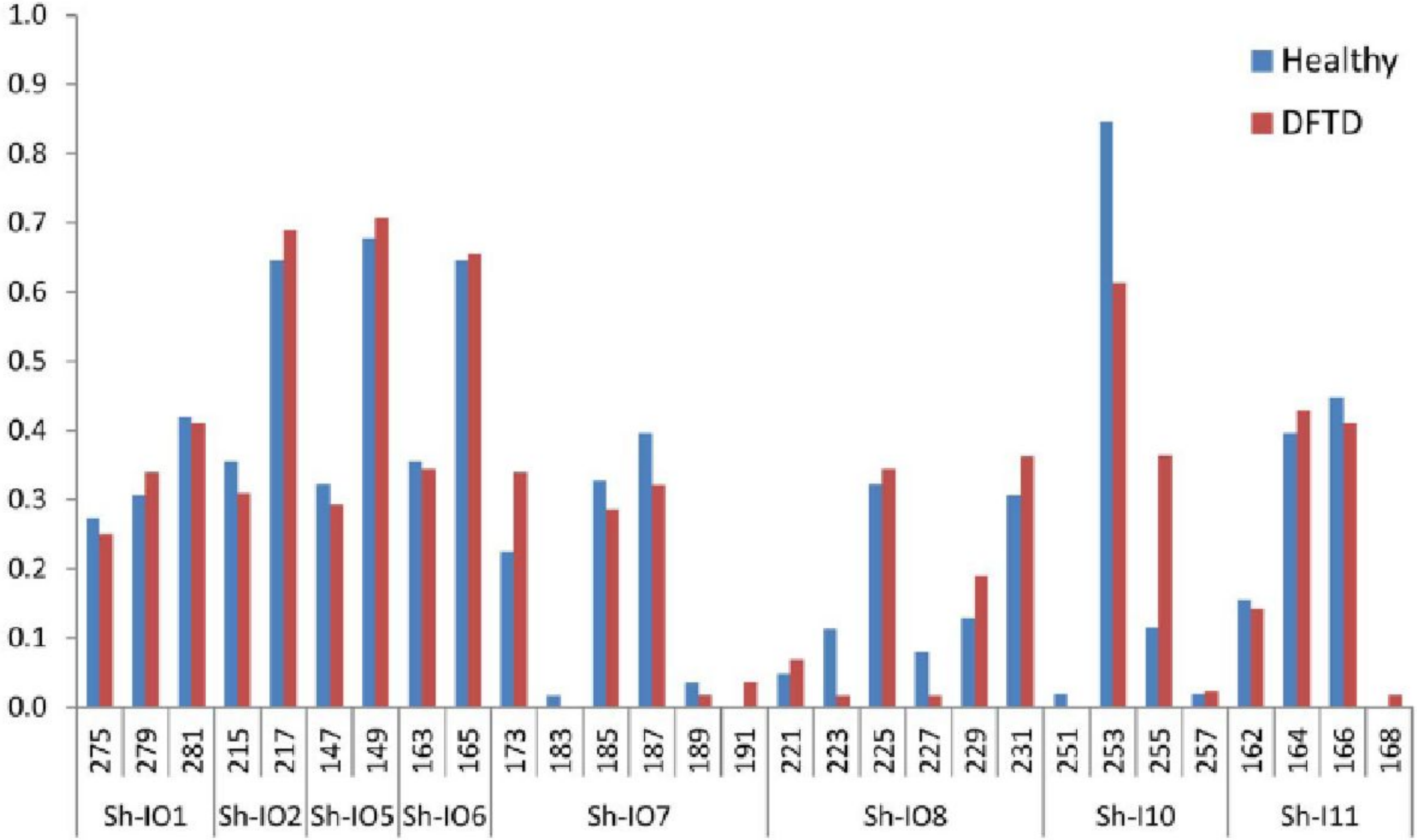


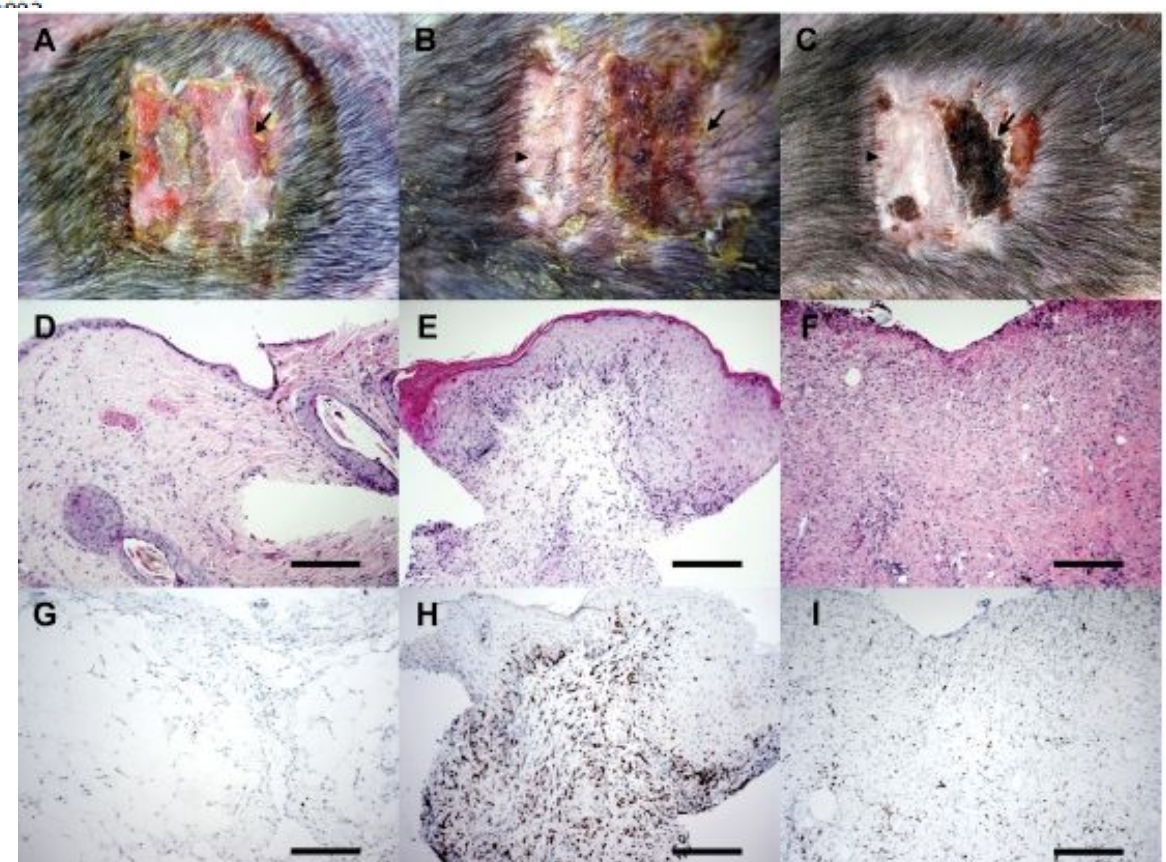
Figure 2. MHC-linked microsatellite loci allele frequencies showing little variation between healthy and DFTD infected devils.

Отторжение аллографтов у тасманского дьявола

Table 2. Outcome of skin allografts.

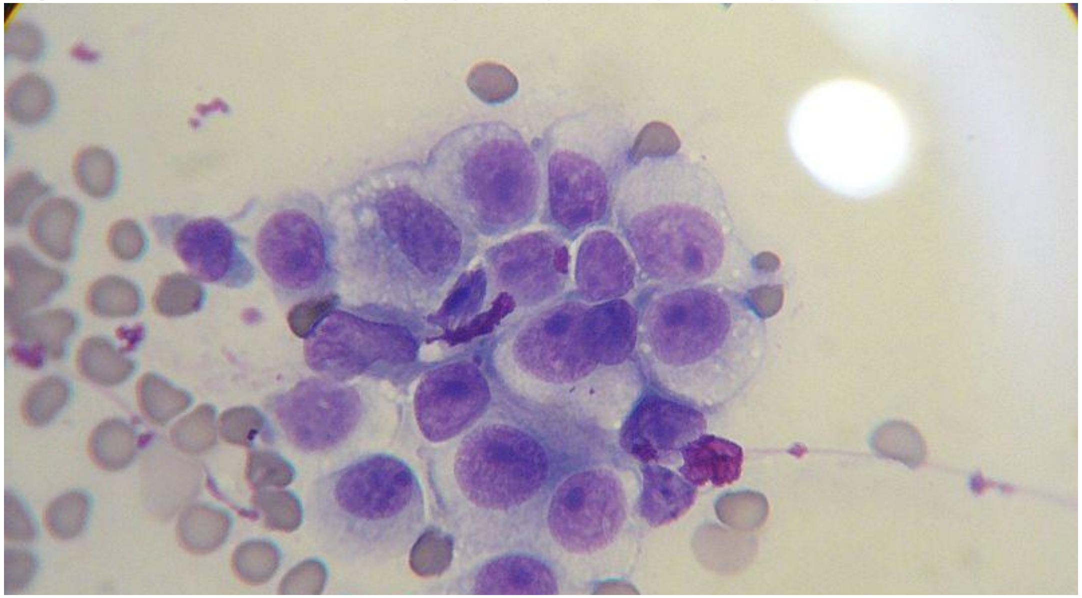
Tasmanian devil ID	Day 7	Day 14	Day 21
TD 190	Grade II	Grade IV	Necrotic skin, biopsy not done
TD 199	No evidence of rejection	Grade III	Grade IV
TD 187	Unable to determine rejection	Grade IV	Necrotic skin, biopsy not done
TD 188	No evidence of rejection	Grade III	Grade IV
TD 191	No evidence of rejection	Grade III	Necrotic skin, biopsy not done

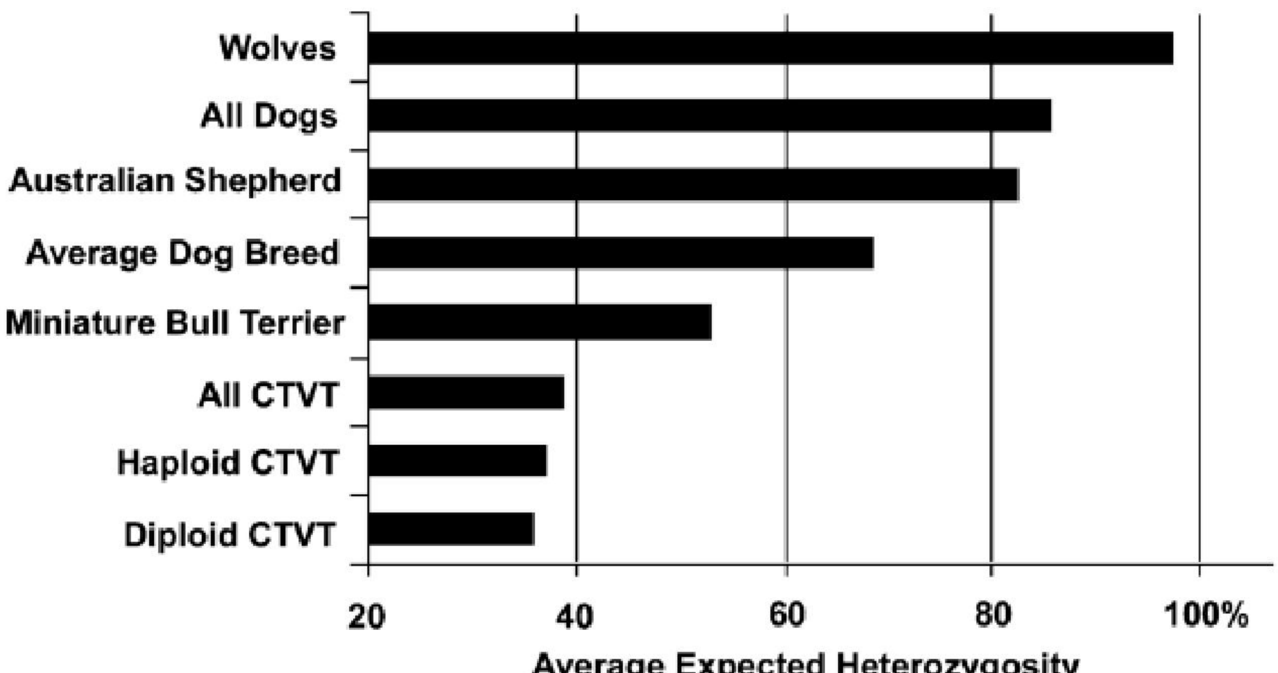
TD 190 was the only devil that showed an early rejection response at Day 7. All five devils had Grade III to Grade IV rejection at Day 14 and Day 21.



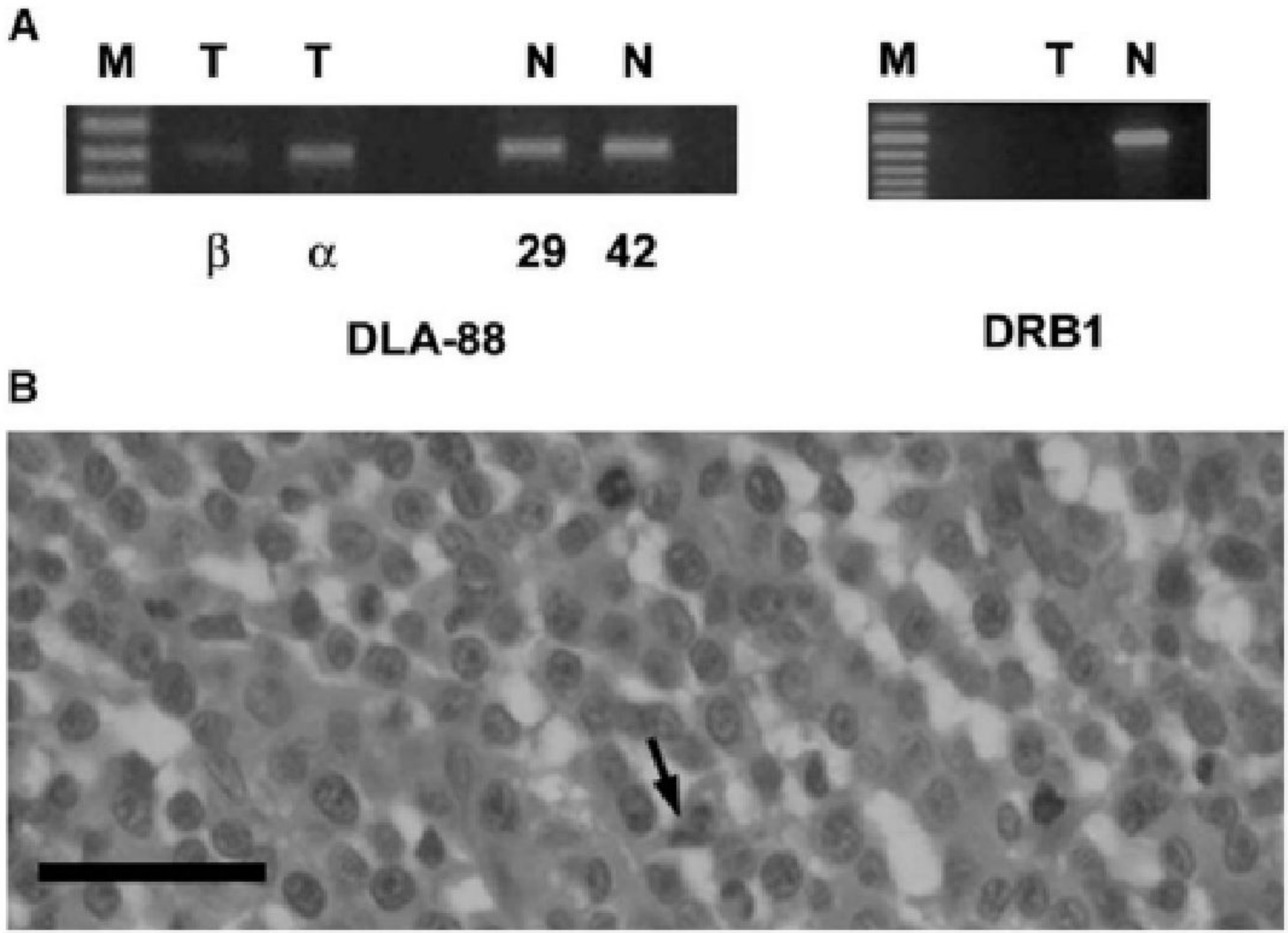
Венерически передаваемая опухоль собак - CTVT

CTVT высоко гомозиготна

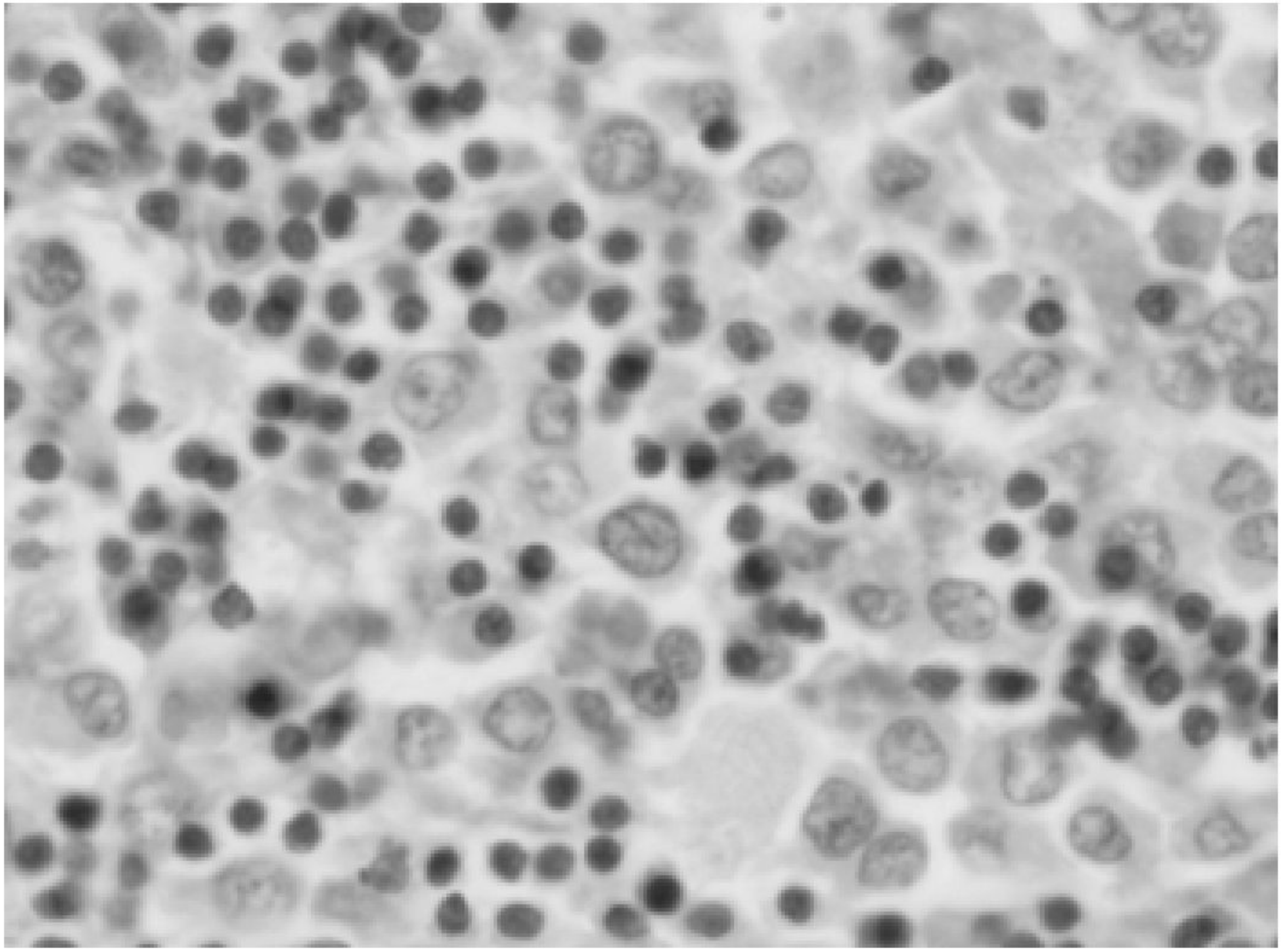




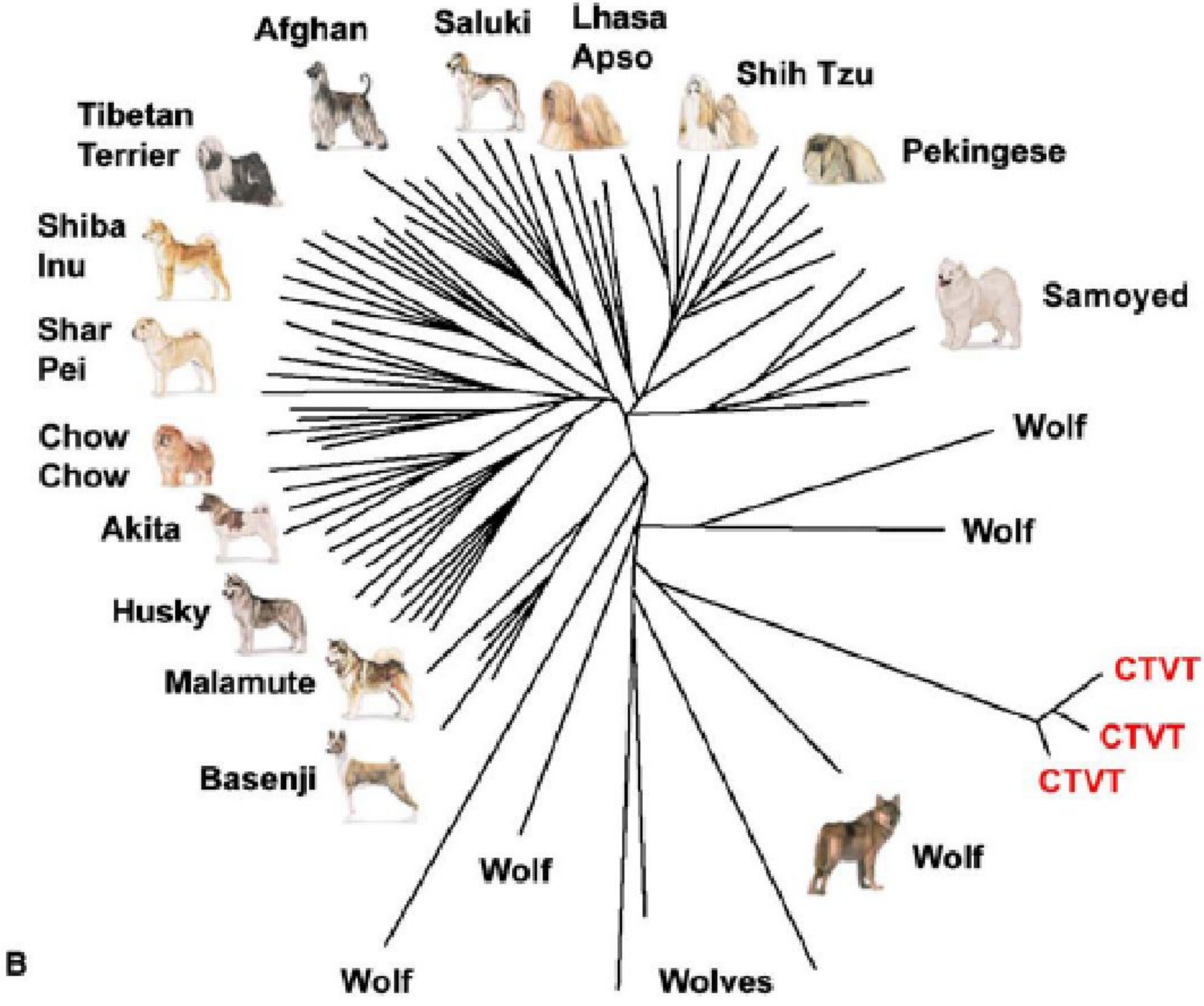
Стадия прогрессии CTVT и сниженная экспрессия MHC



Стадия регрессии CTVT



Происхождение CTVT и передача от волка собаке



Саркома Стикера гетерогенна по митохондриальной ДНК

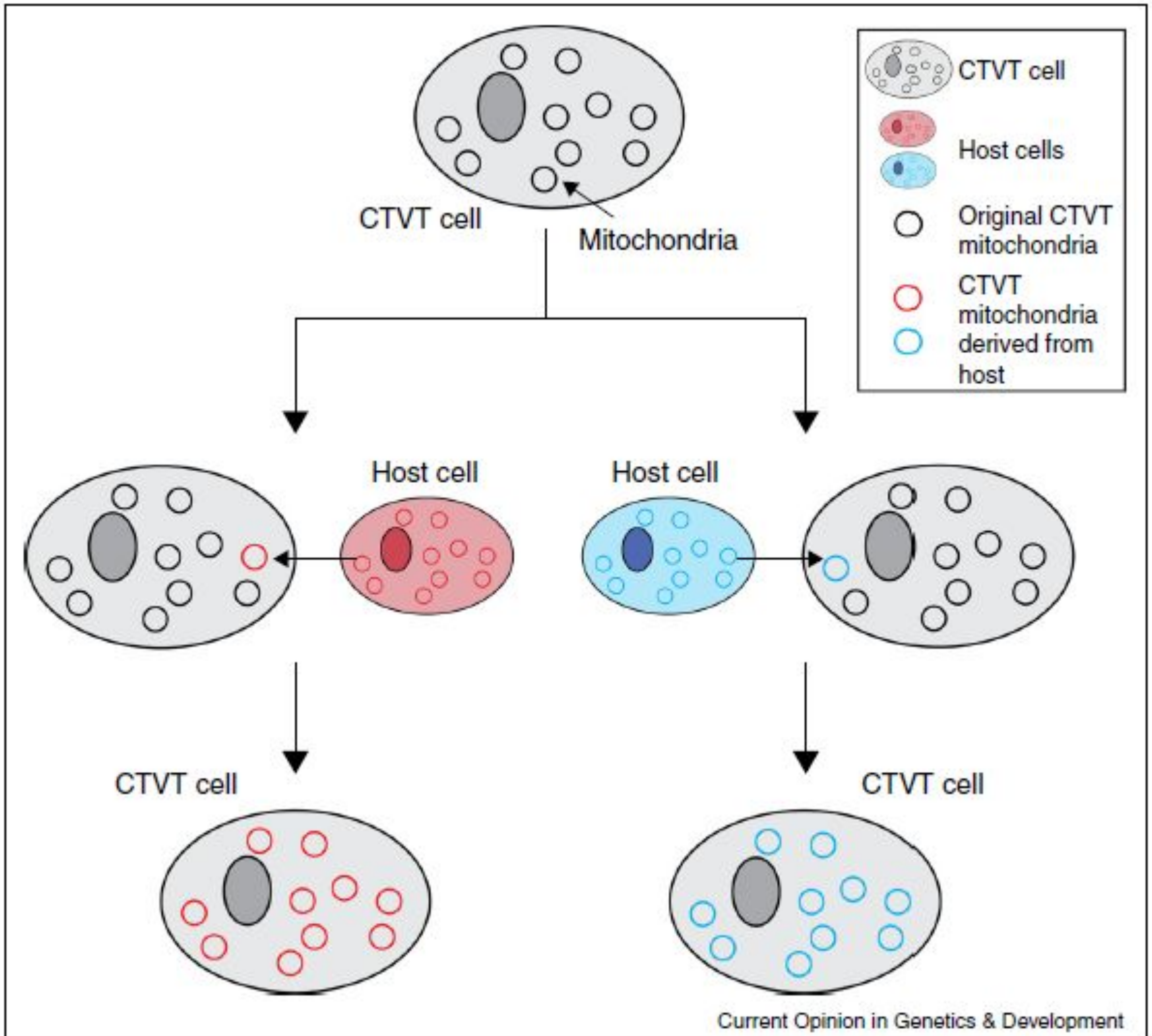
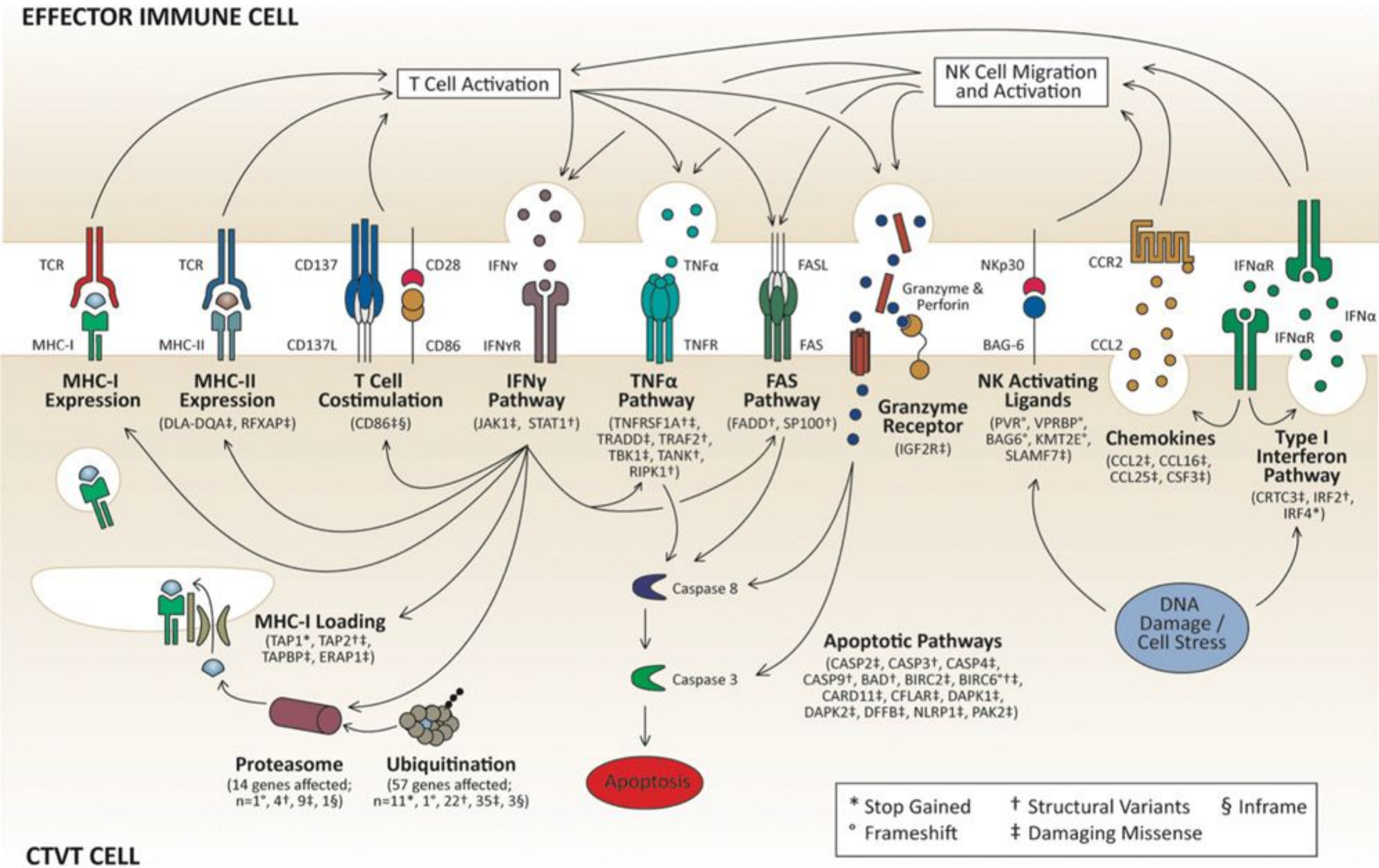


Table 2 Comparison of DFTD and CTVT

	DFTD	*CTVT*
Host species	Tasmanian devil	Dog
Species of origin	Tasmanian devil	Wolf or dog
Distribution	Mainland Tasmania (excluding northwest)	Worldwide
Time of origin	15–20 years ago	7800–78 000 years ago
Body location	Face, oral cavity	External genitalia
Mode of transfer	Biting	Coitus
Histogenesis	Neuroendocrine	Myeloid
Metastasis	Common	Common in immune-compromised animals
Spontaneous regression	0%	Common in experimentally inoculated CTVT, prevalence in naturally occurring CTVT unknown
Mortality	100%, within 6–12 months after appearance of symptoms	Rare in experimentally inoculated CTVT, prevalence in naturally occurring untreated CTVT unknown
Treatment	None	Chemotherapy, radiation therapy
Effect on host population	Host population decline/possible imminent extinction	Probably little effect

Многие гены CTVT несут мутации потери функции



На самом деле, устойчивость DFTD вызвана эпигенетическим подавлением экспрессии TAP1, TAP2 и β2-микроглобулина, что ведет к снижению у нее количества MHC I

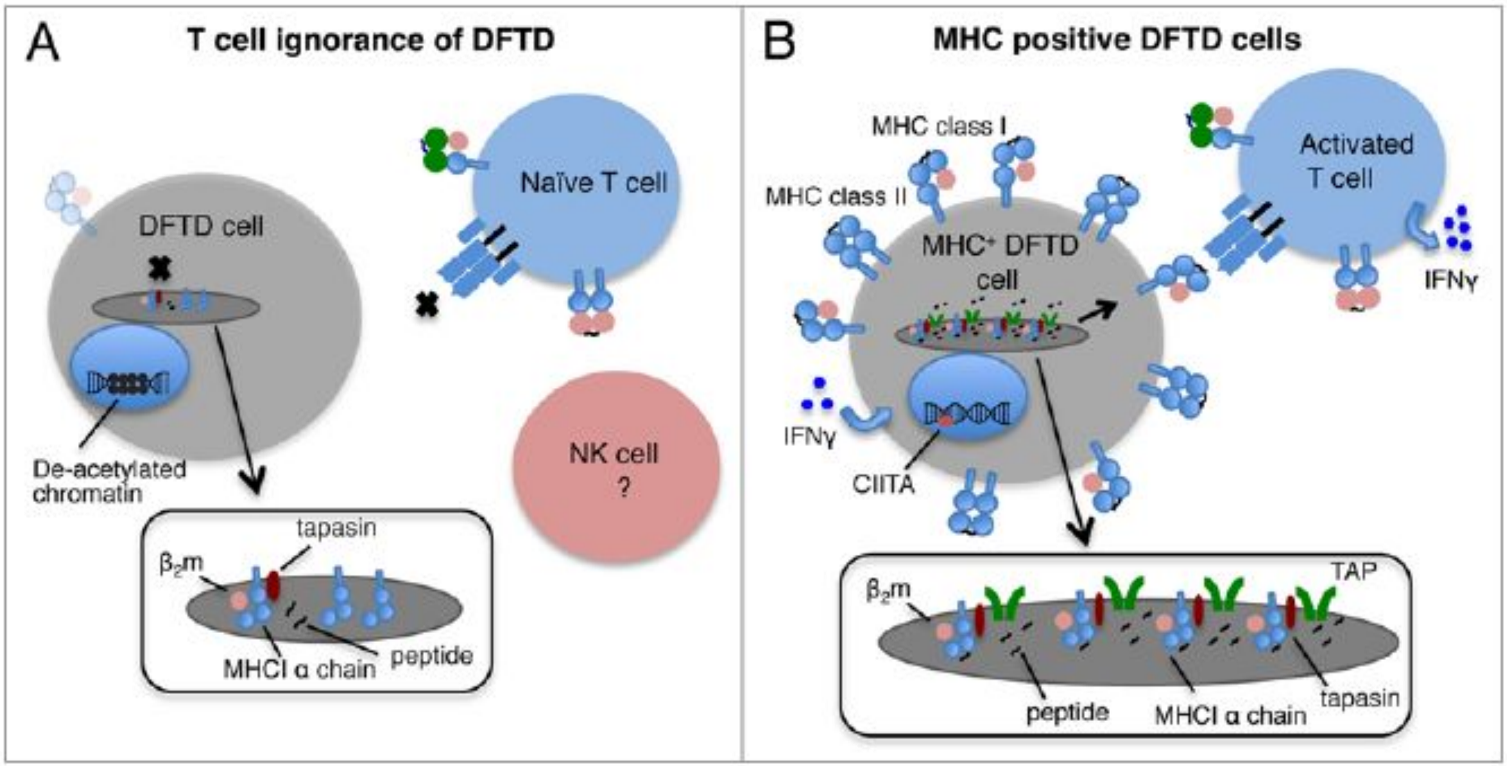
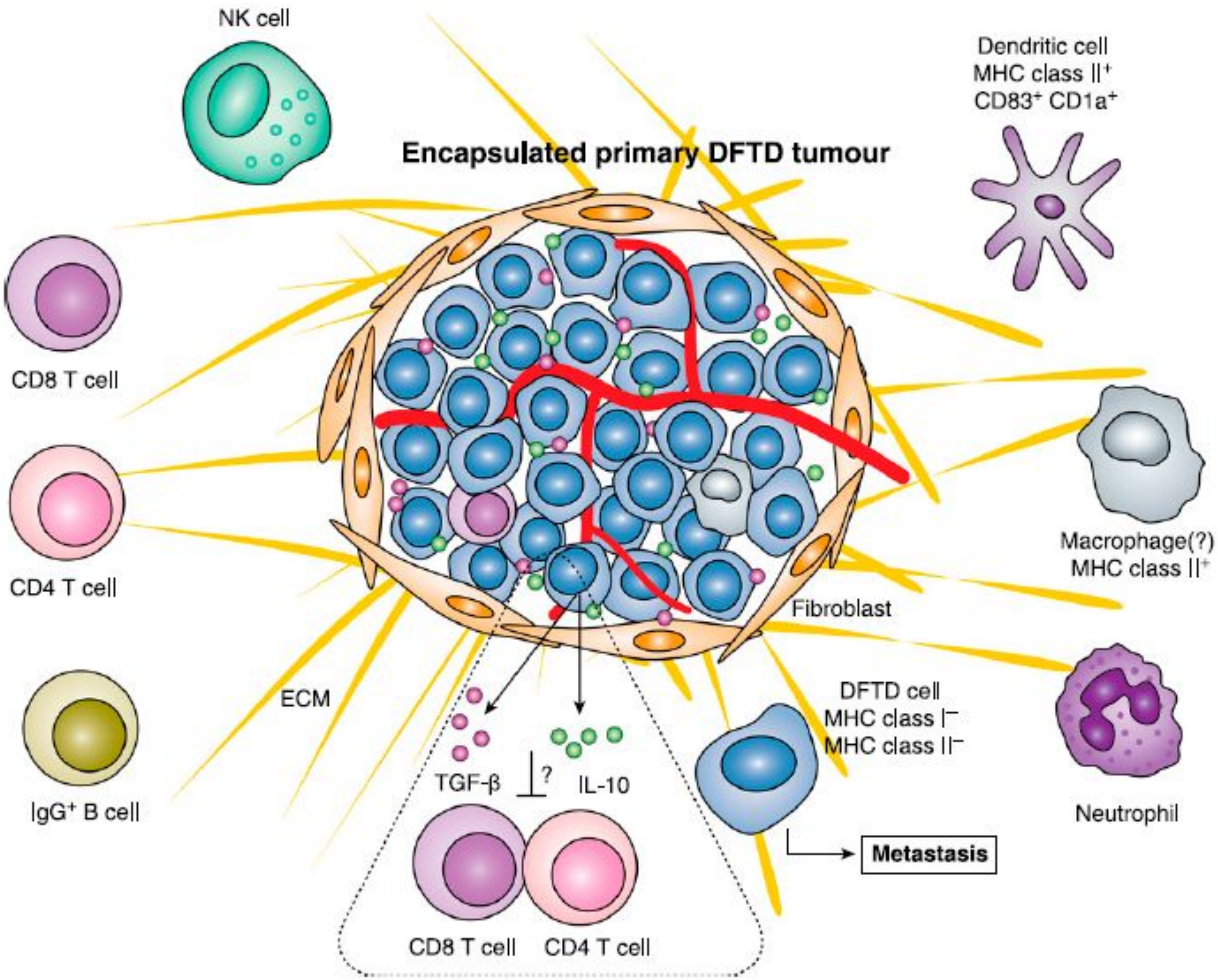
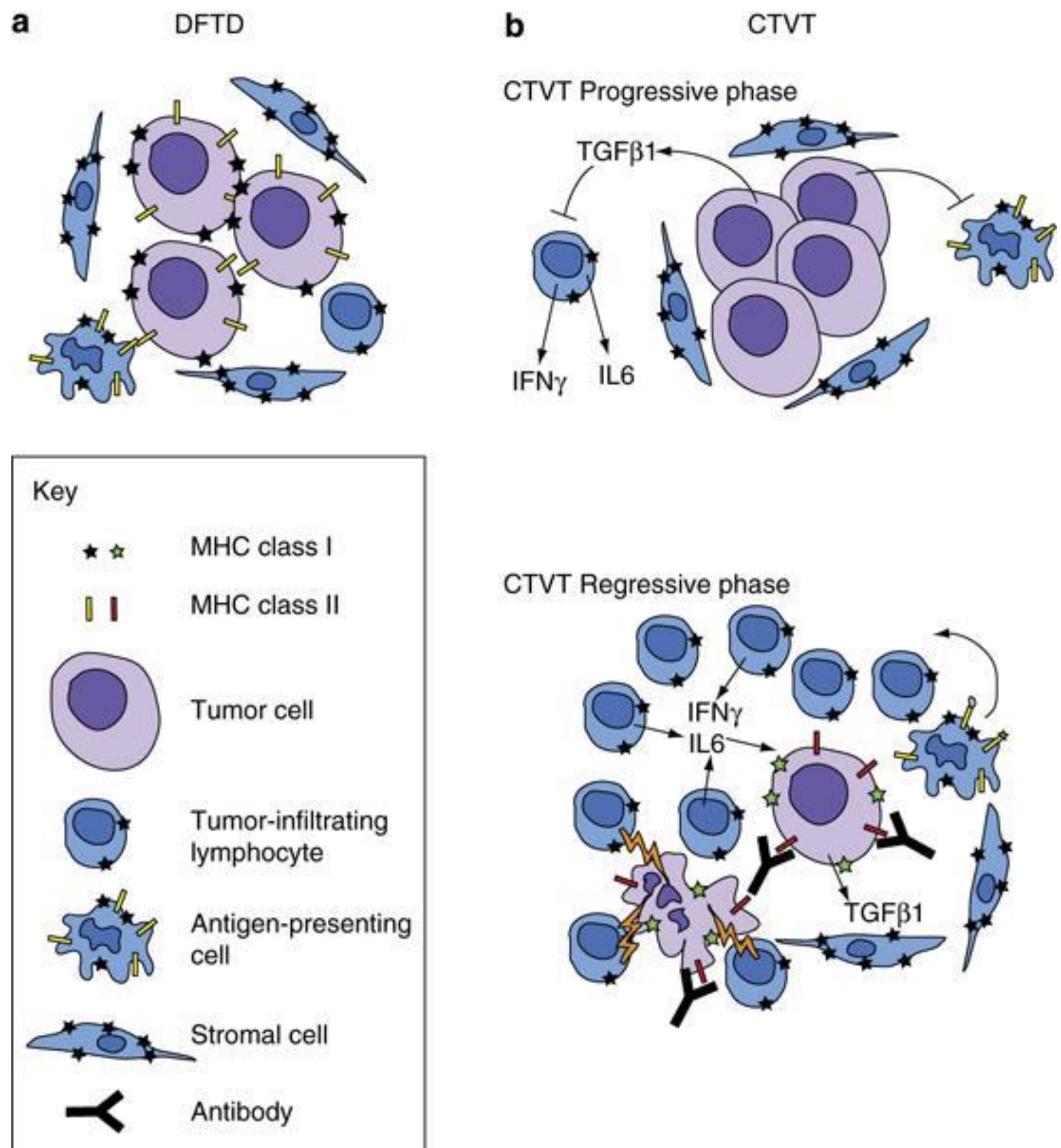


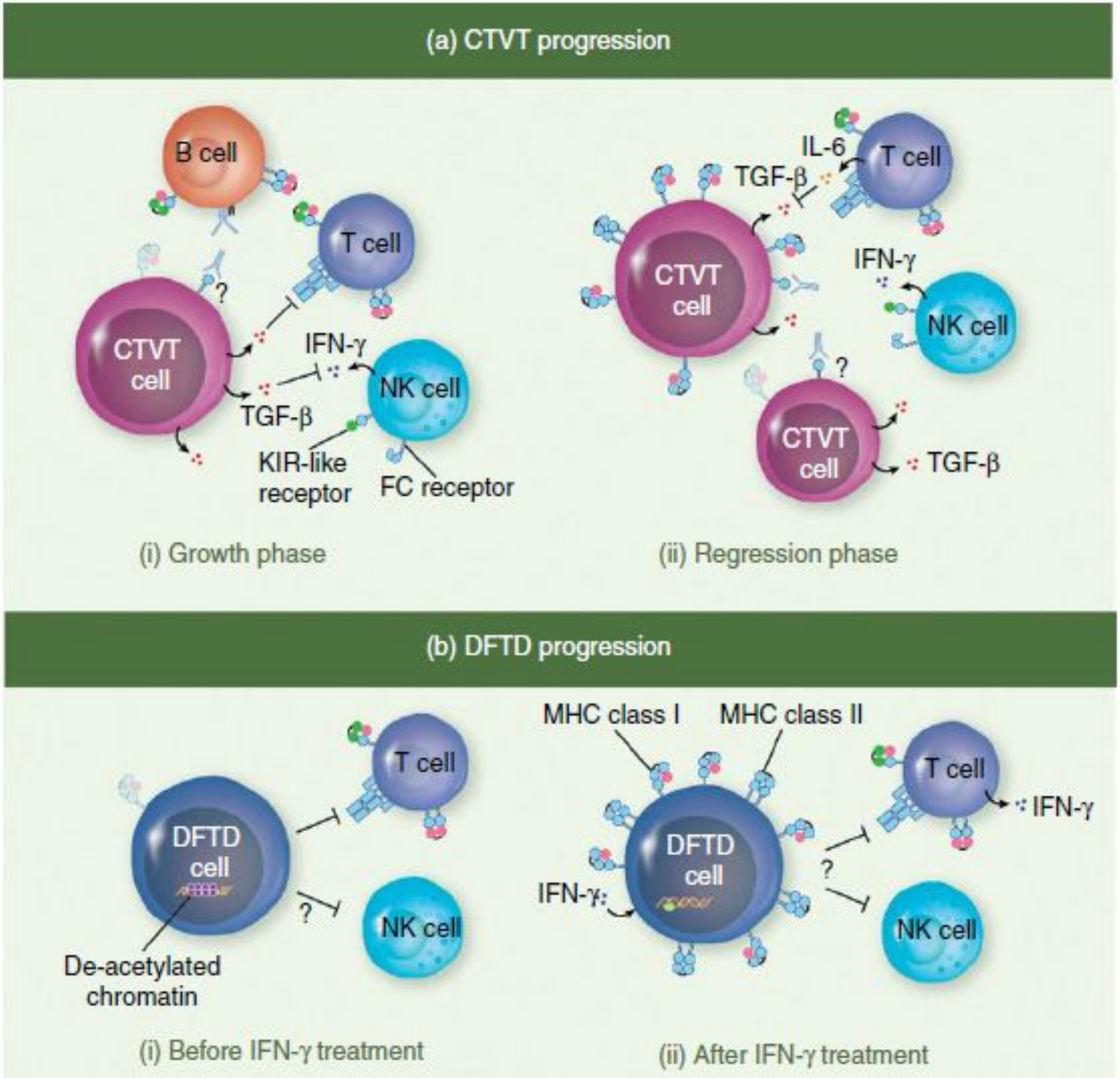
Figure 1. Mechanisms of immune evasion by DFTD cells. (**A**) Devil T lymphocytes fail to recognize devil facial tumor disease (DFTD) cells as the latter lack MHC molecules on their surface. This is mainly due to the deacetylation-dependent repression of transcription from β_2-microglobulin (β_2m), transporter associated with antigen presentation (TAP) 1 and TAP2-coding genes. In this situation, MHC Class I heavy chains are produced but retained in the endoplasmic reticulum (ER). Low levels of MHC Class I molecules may be found on the surface of DFTD cells owing to the synthesis of trace amounts of β_2m and to peptides derived from ER-resident proteins. (**B**) DFTD cells can re-express MHC Class I molecules on their surface. Upon interferon γ (IFNγ) treatment of DFTD cells, β_2m, TAP1, TAP2, MHC Class II molecules and the transcription factor Class II transactivator (CIITA) are upregulated and MHC Class I molecules are expressed on the cell surface. Devils vaccinated with MHC Class I-expressing DFTD cells are expected to activate a protective T-cell response. Insets represent magnified view of the ER.

Толерогенное действие клеток DFTD



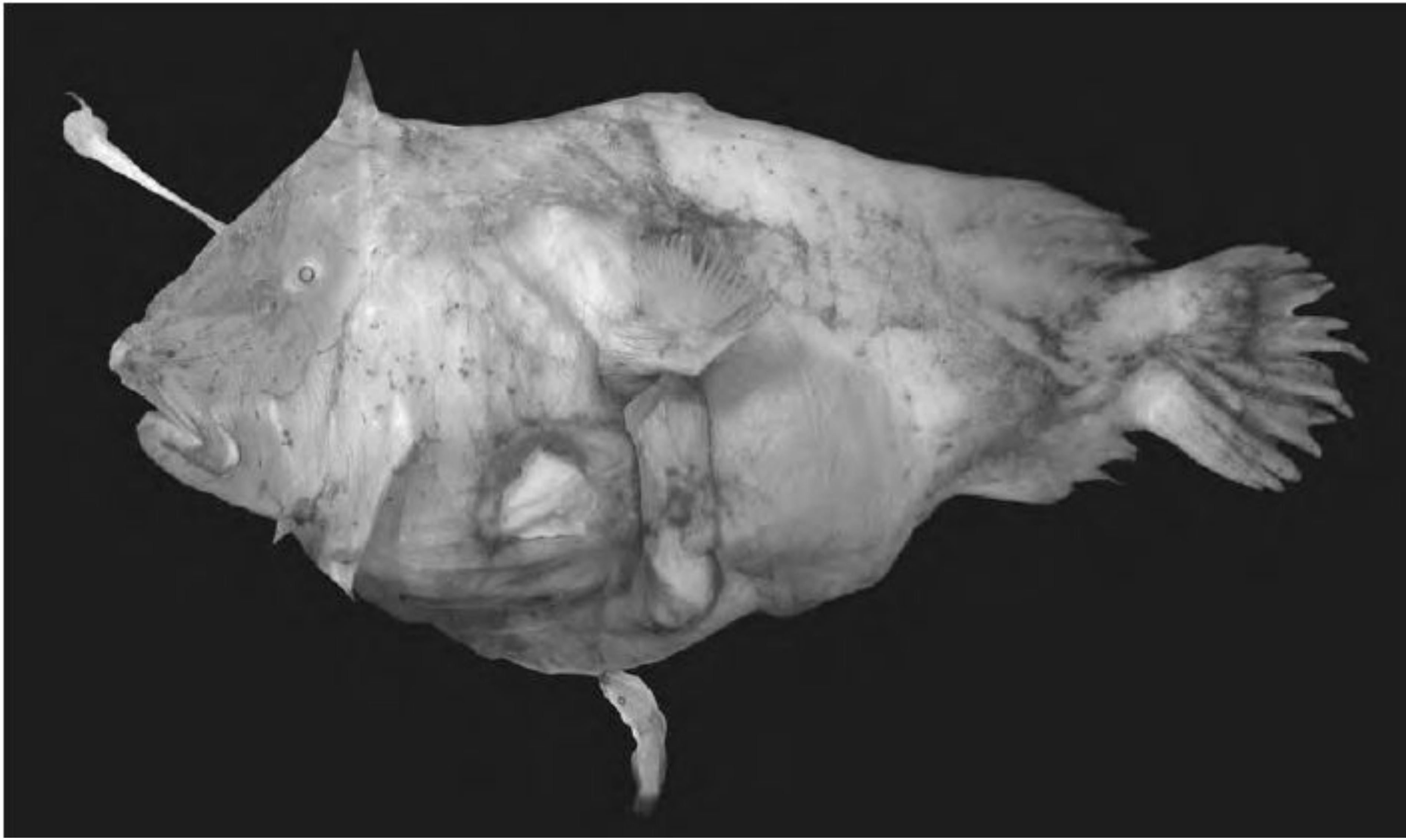
Сравнение DFTD и CTVT





(a) CTVT progression
B cell
T cell
CTVT cell
?
IFN-γ
NK cell
TGF-β
KIR-like receptor
FC receptor
(i) Growth phase
IL-6
T cell
TGF-β
CTVT cell
IFN-γ
NK cell
?
CTVT cell
TGF-β
(ii) Regression phase
(b) DFTD progression
T cell
DFTD cell
?
NK cell
De-acetylated chromatin
(i) Before IFN-γ treatment
MHC class I
MHC class II
T cell
IFN-γ
DFTD cell
IFN-γ
?
NK cell
(ii) After IFN-γ treatment

Паразитизм карликовых самцов удильщиков – потенциальная иммунологическая модель?



Ткани самца и самки удильщиков срастаются

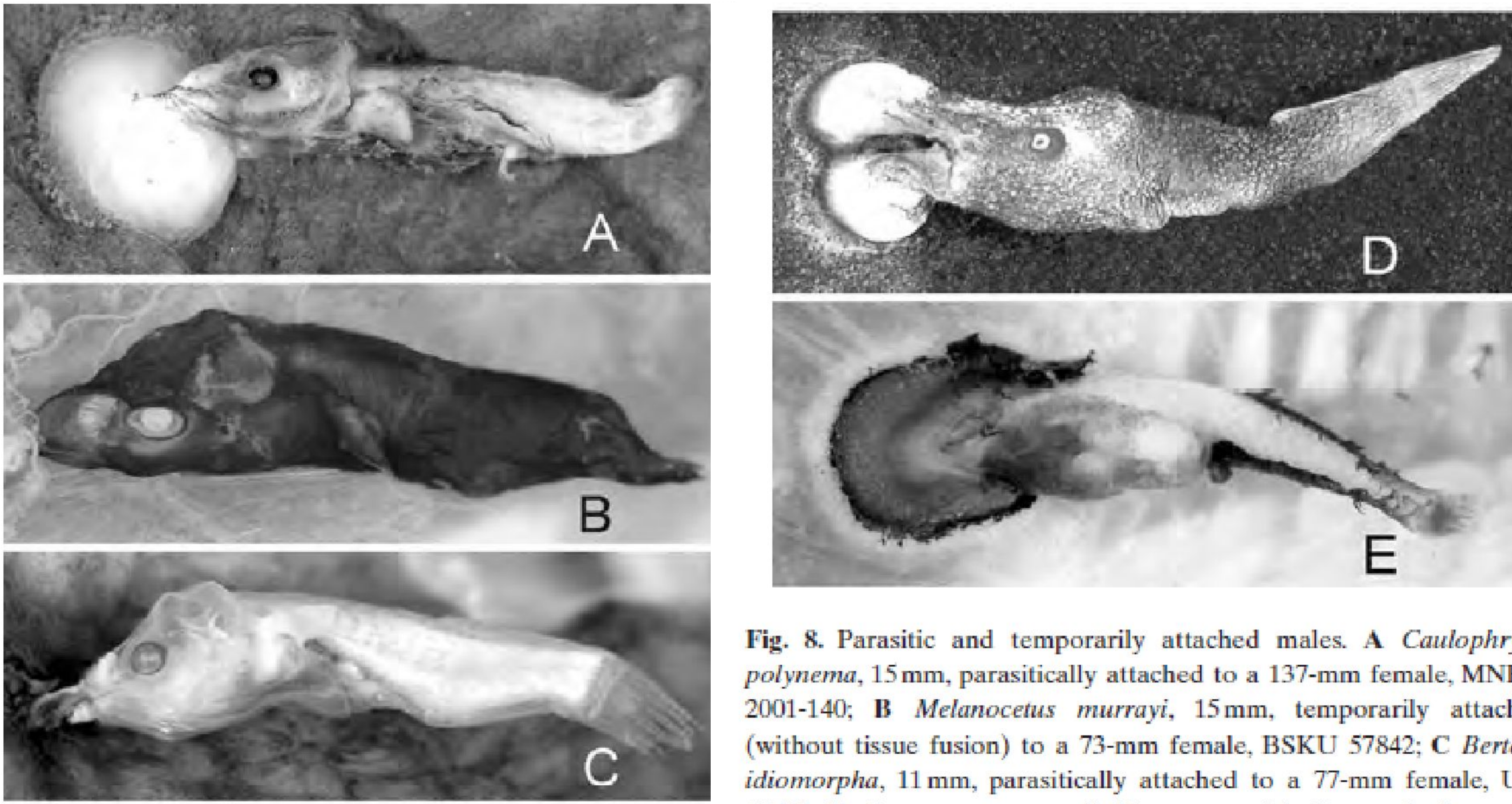


Fig. 8. Parasitic and temporarily attached males. **A** *Caulophryne polynema*, 15 mm, parasitically attached to a 137-mm female, MNHN 2001-140; **B** *Melanocetus murrayi*, 15 mm, temporarily attached (without tissue fusion) to a 73-mm female, BSKU 57842; **C** *Bertella idiomorpha*, 11 mm, parasitically attached to a 77-mm female, UW 48712; **D** *Cryptopsaras couesii*, 10 mm, parasitically attached to a 45-mm female, ARC 8707665; **E** *Neoceratias spinifer*, 18 mm, parasitically attached to a 108-mm female, SIO 70-336

- Следующая лекция 2 апреля – об иммунитете Круглоротых