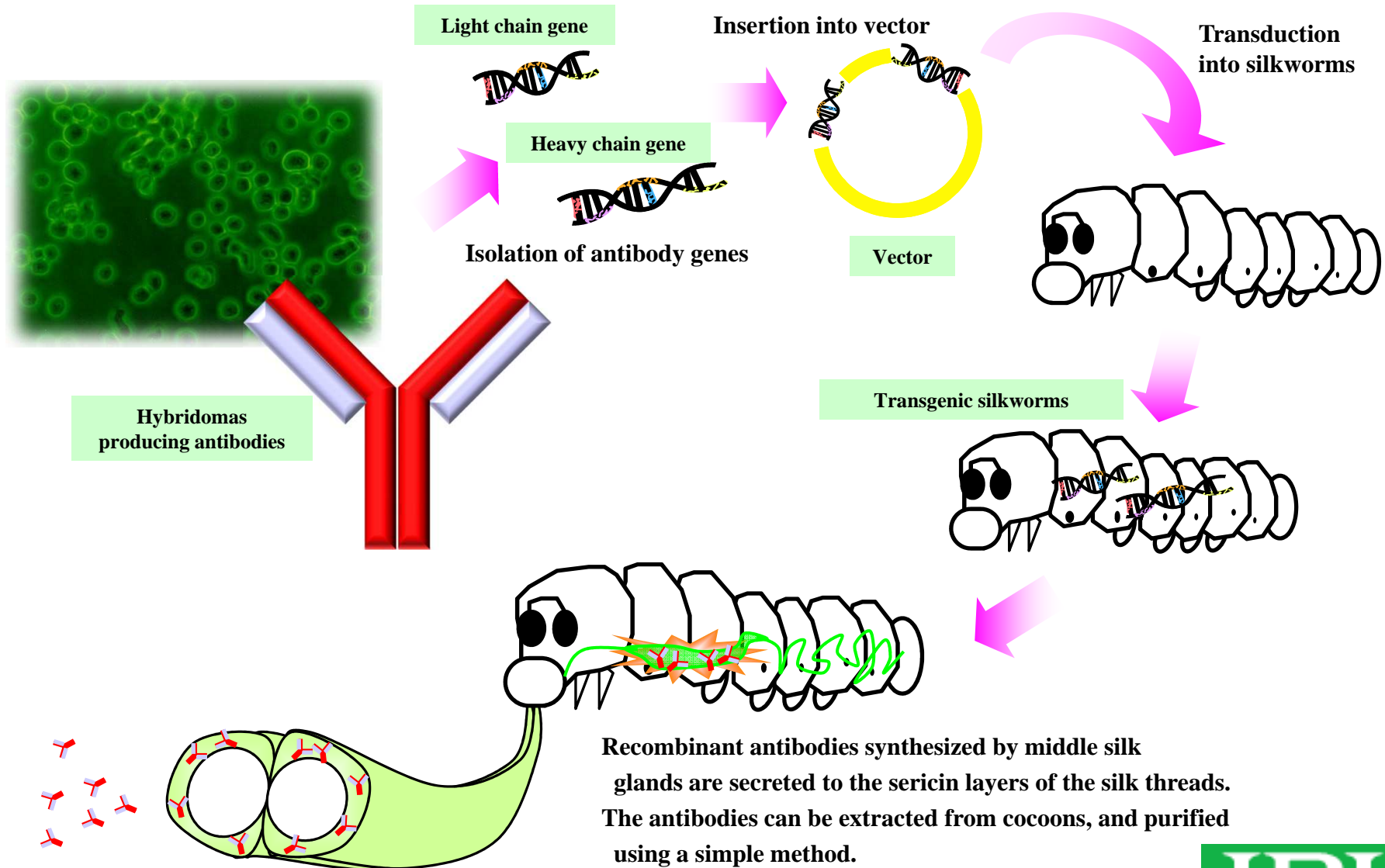


Transgenic (TG) silkworms that produce recombinant monoclonal antibodies

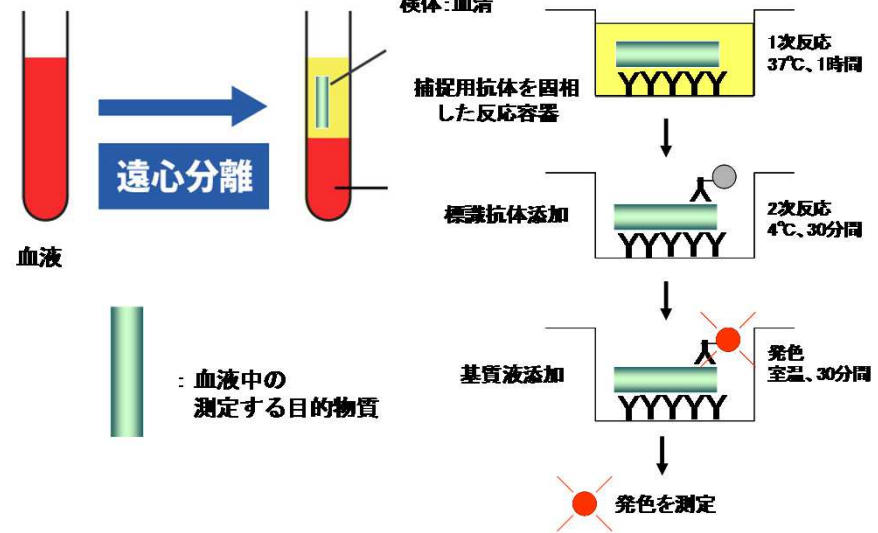
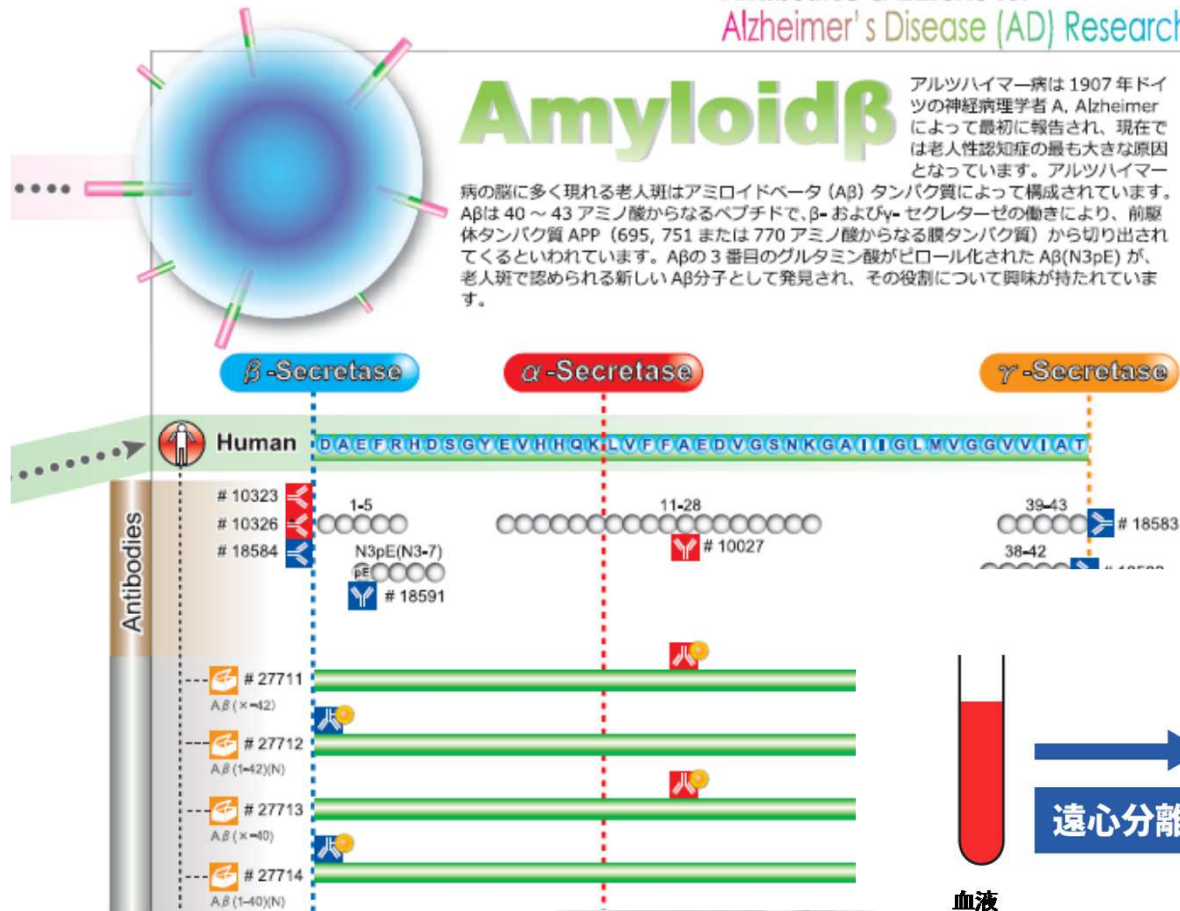


Changeover of antibodies for ELISA kit: From mice to silkworms

Antibodies & ELISAs for Alzheimer's Disease (AD) Research

Amyloid β

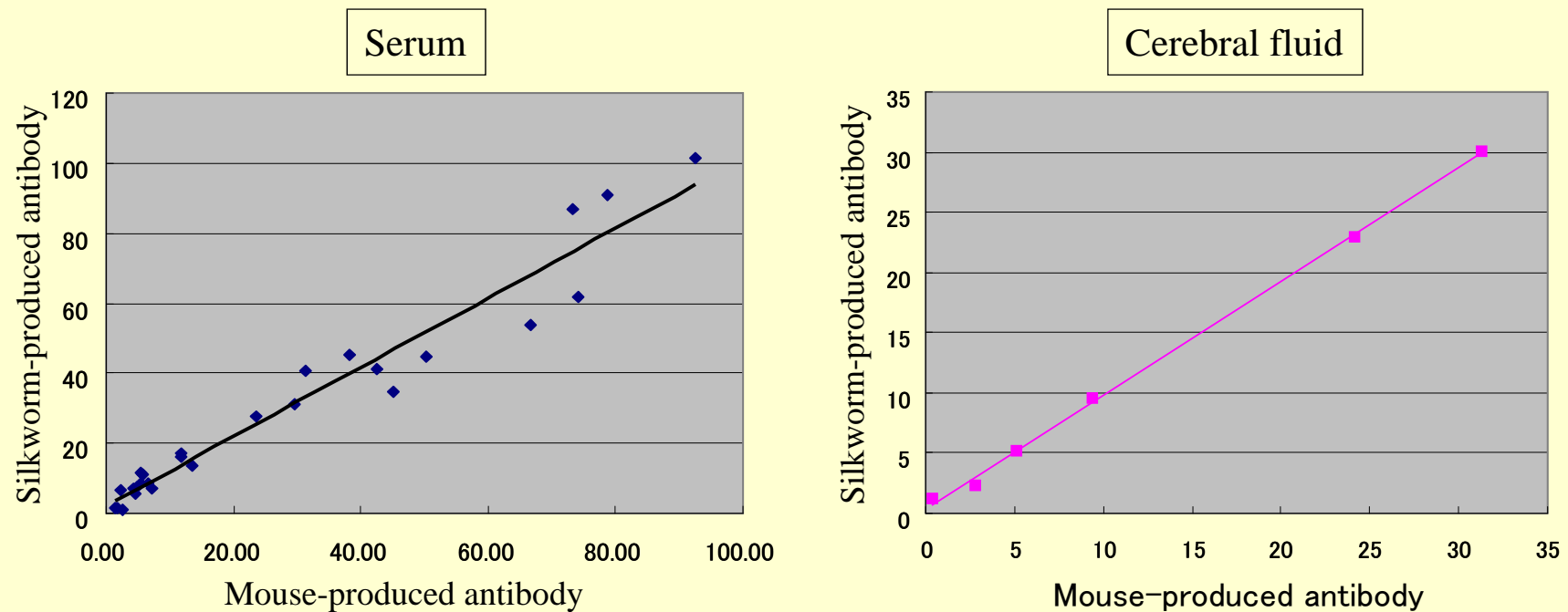
アルツハイマー病は1907年ドイツの神経病理学者 A. Alzheimer によって最初に報告され、現在では老人性認知症の最も大きな原因となっています。アルツハイマー病の脳に多く現れる老人斑はアミロイドベータ (A β) タンパク質によって構成されています。A β は40~43アミノ酸からなるペプチドで、 β -および γ -セクレターゼの働きにより、前駆体タンパク質 APP (695, 751 または 770 アミノ酸からなる膜タンパク質) から切り出されてくるといわれています。A β の3番目のグルタミン酸がピロール化された A β (N3pE) が、老人斑で認められる新しい A β 分子として発見され、その役割について興味を持たれています。



血液中の測定する目的物質

Performance of silkworm-produced anti-amyloid β

Correlation of reactivity between silkworm- and mouse-produced antibodies



High correlation was observed.

Additional merits

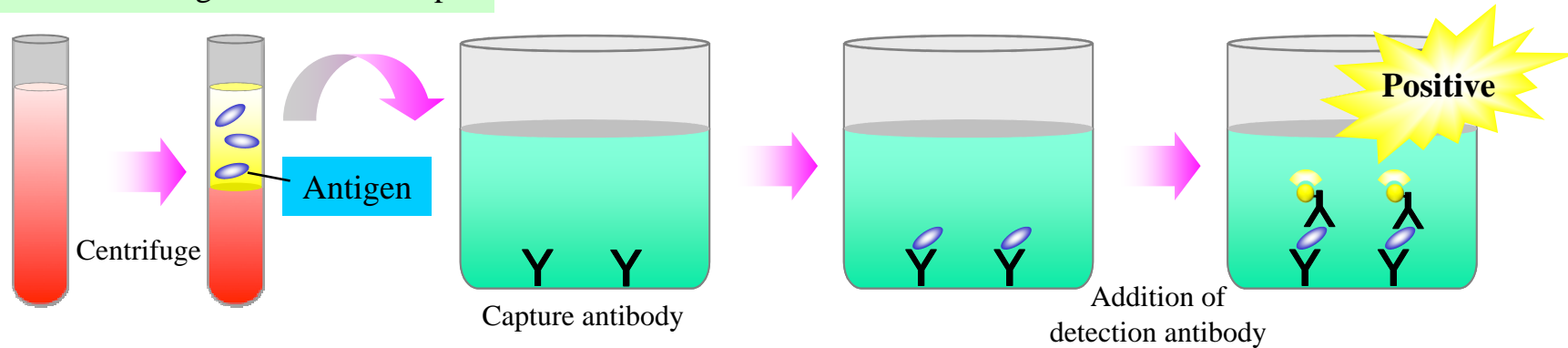
- **Low production cost**
- **Production of high quality antibodies with lot-to-lot consistency**

Issue of false-positive reaction caused by HAMA

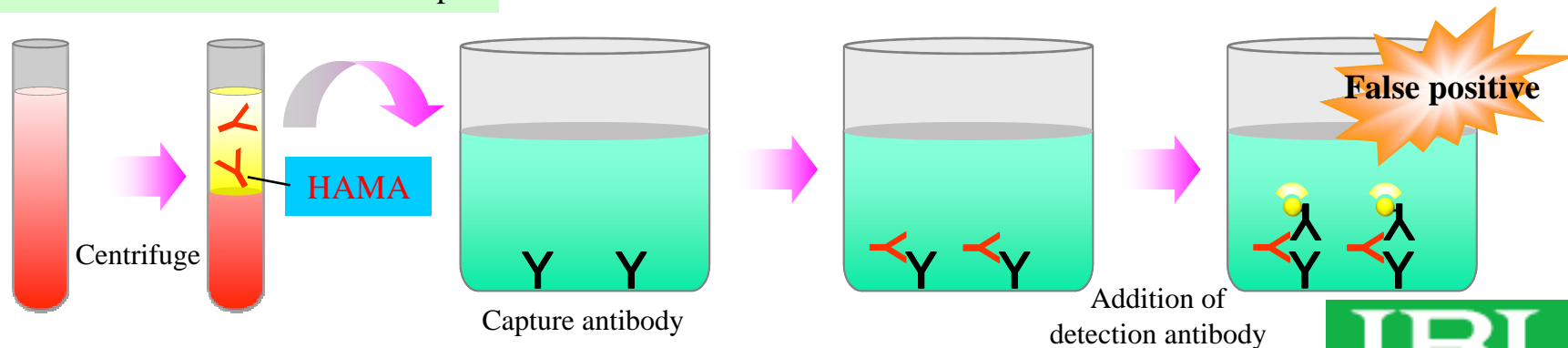
HAMA (Human Anti-Mouse Antibody)

- Human antibody recognizes mouse antibody as an antigen
- Detection rate in human serum samples: A few percent to a few dozen percent
- Cause of false-positive reaction in two-site ELISA

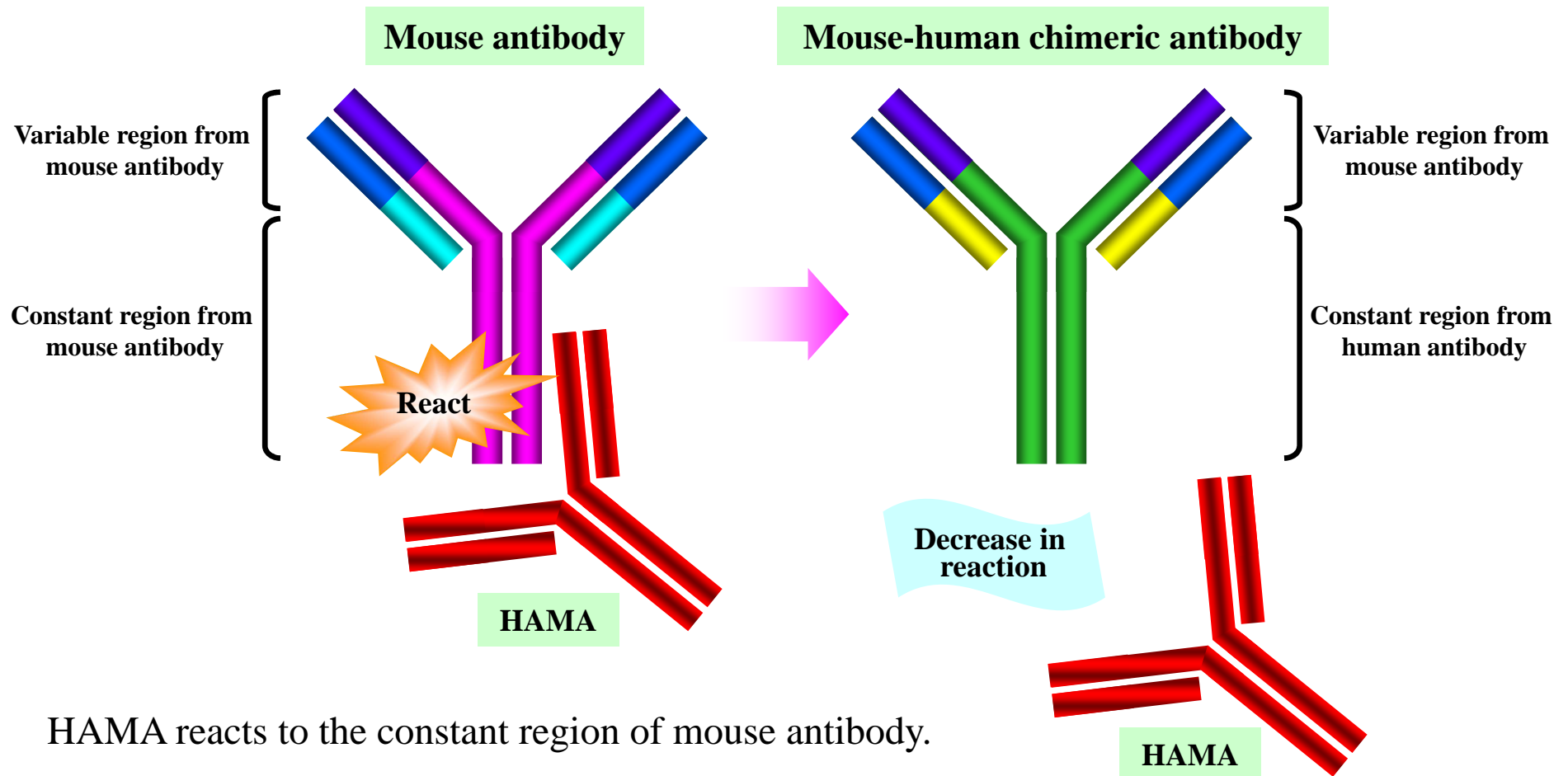
Presence of antigen in serum sample



Presence of **HAMA** in serum sample



Inhibition of HAMA-reaction by using mouse-human chimeric antibody

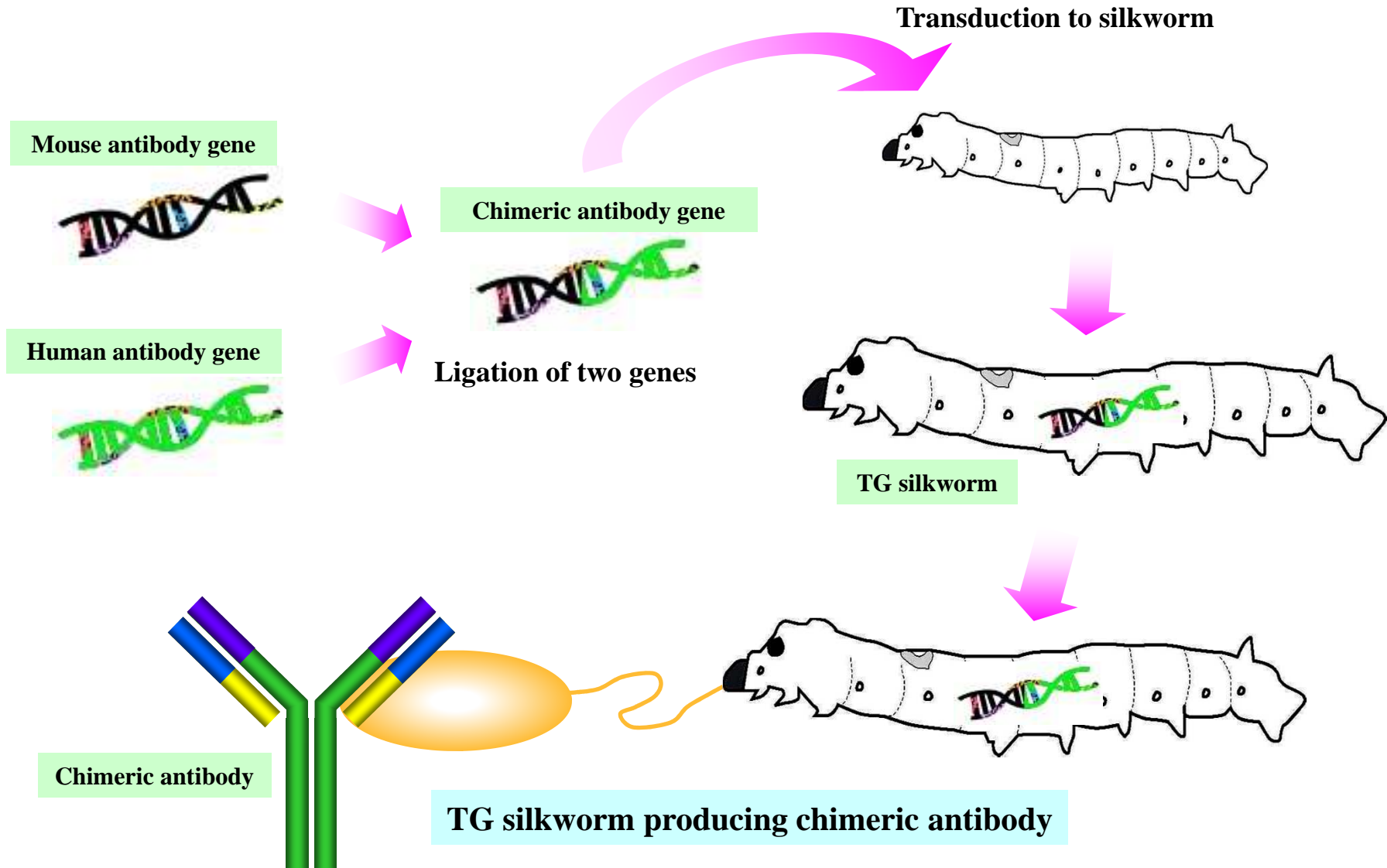


HAMA reacts to the constant region of mouse antibody.

HAMA-reaction is inhibited by using a mouse-human chimeric antibody in which the constant region of the mouse antibody is replaced by the constant region of the human antibody.



TG silkworm producing chimeric antibody

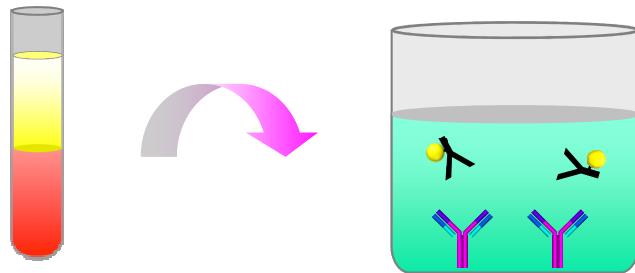


Evaluation of TG silkworm-produced chimeric antibody

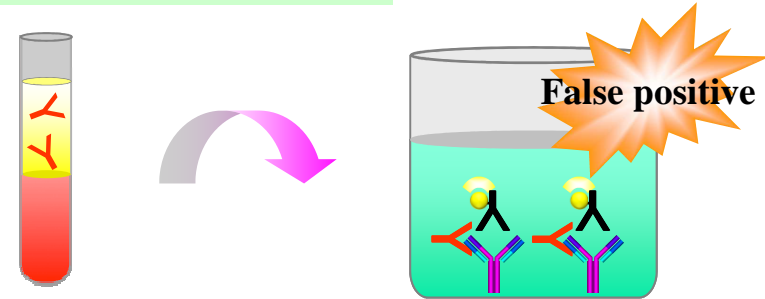
ELISA system was constructed by using two independent antibodies which each react to different antigens.

The chimeric antibody was used as a capture antibody.

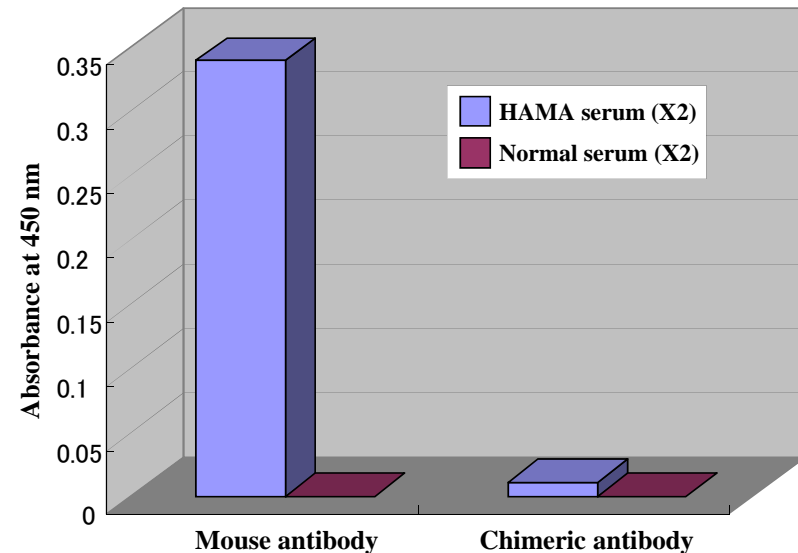
Normal serum



HAMA-containing serum



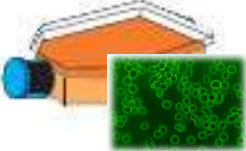

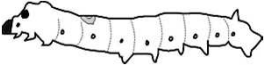
Deletion	Mouse antibody		Chimeric antibody	
	HAMA serum	Normal serum	HAMA serum	Normal serum
× 2	0.340	-0.005	0.012	-0.003
× 4	-0.005	-0.008	0.002	0.000
× 8	-0.006	0.000	0.012	0.005
× 16	-0.004	-0.006	0.014	0.016
× 32	-0.008	-0.005	0.008	0.003
× 64	-0.004	-0.004	0.006	0.006
× 128	0.495	-0.003	0.005	0.003
blank	0.007	0.003	0.006	0.000



HAMA-reactivity decreased to 3% of that for mouse antibody.



Comparison to other antibody production system

		Cost	Lot-to-lot consistency	Production period	Ethical problem
	Hybridoma culture	High	Relatively low	Short	No
	Mouse ascites	Low	Low	Short	Yes
	TG silkworm	Low*	High	Long at first production	No

*Production cost in TG silkworm is nearly comparable to the production of mice ascites.

Antibody production using TG silkworms

- Solution for the production of antibodies for diagnostic use -

- **No ethical problems. Best alternative to mice ascites production.**
- **High lot-to-lot consistency. High quality.**
- **Low cost when producing orders of more than a gram.**
- **Low background. Inhibition of HAMA-reaction.**