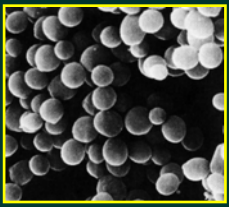
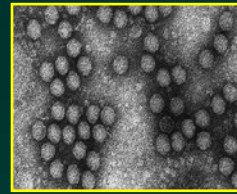


The Antimicrobial Defense of
Drosophila,
A Paradigm for Innate Immunity

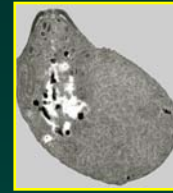
Jules Hoffmann, Strasbourg, France



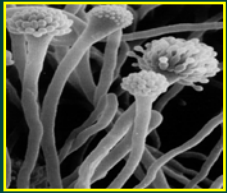
Bacteria



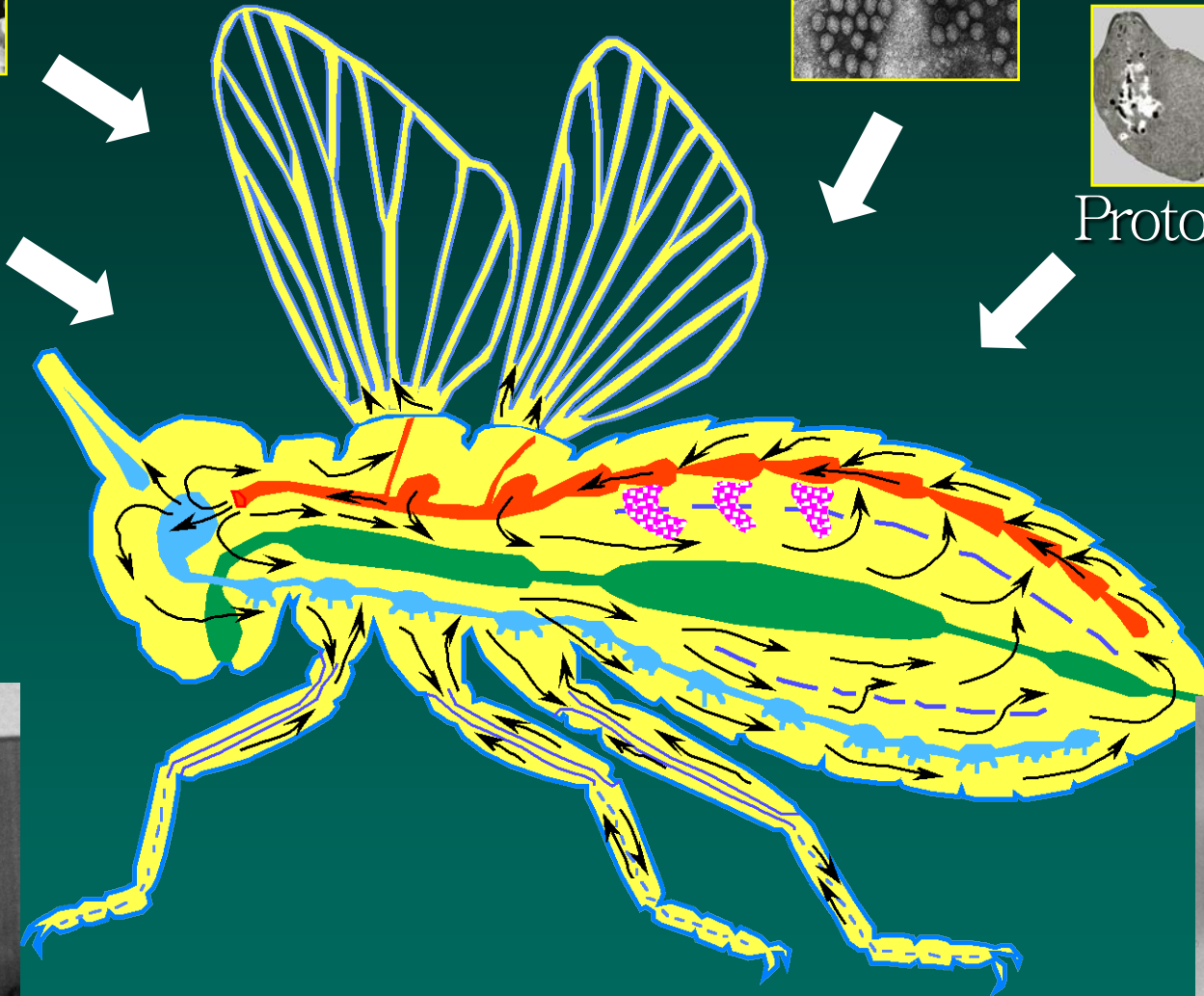
Viruses



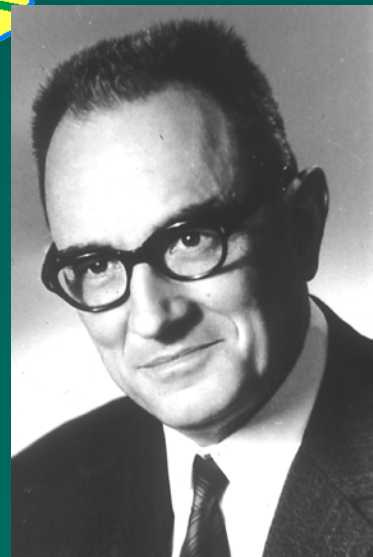
Protozoa



Fungi

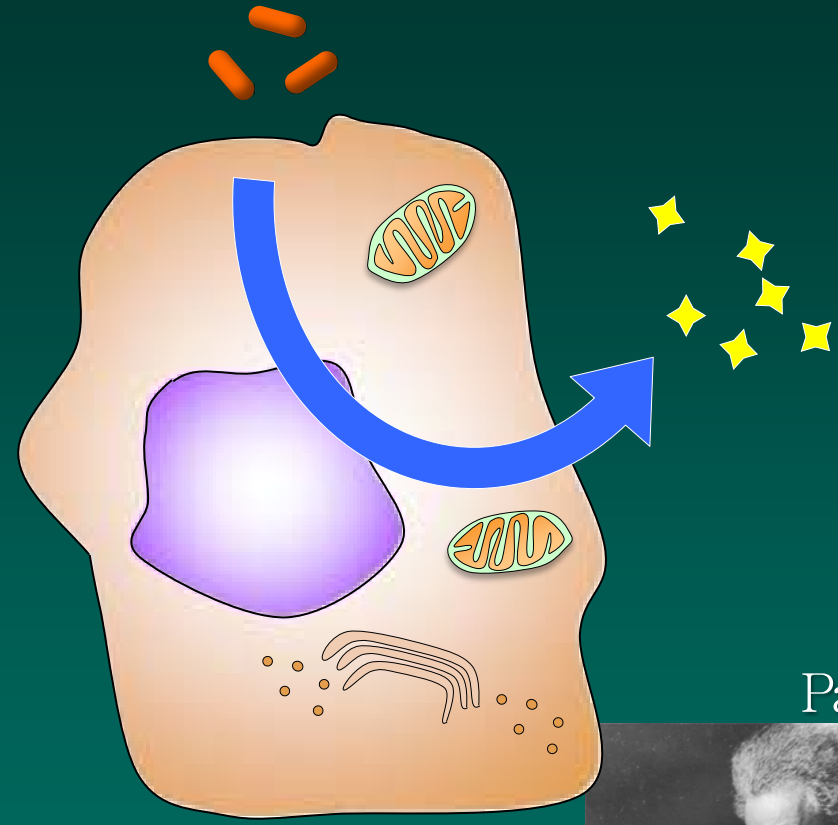
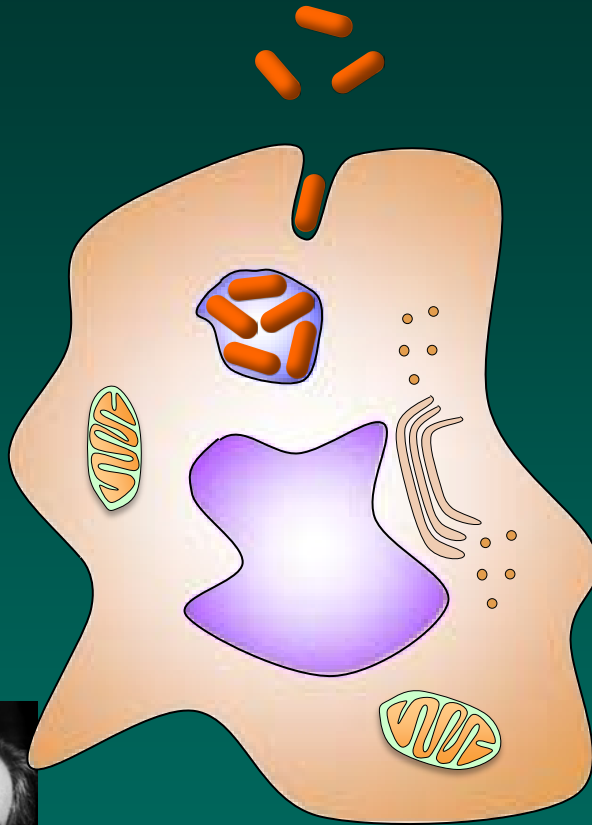


Jos Hoffmann
1911-2000



Pierre Joly
1913-1996

Antimicrobial Defenses in Insects : First Investigations



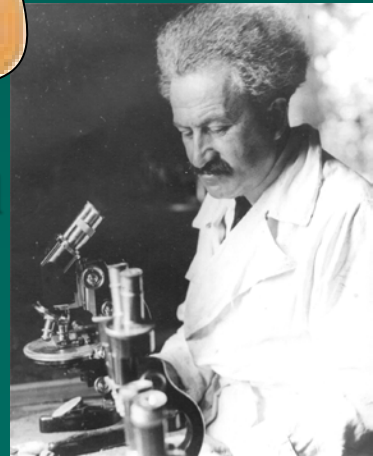
Metchnikoff

Paillot

Phagocytosis

« Cellular Immunity »
Metchnikoff, 1880

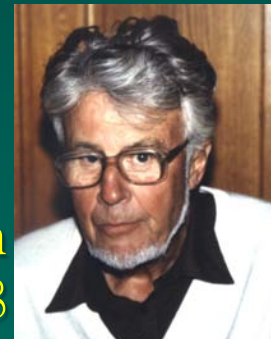
Antimicrobial
substances in the blood
« Humoral Immunity »
Paillot 1920-1935
Glaser



Induction of an antimicrobial activity in *Drosophila* by an immune challenge

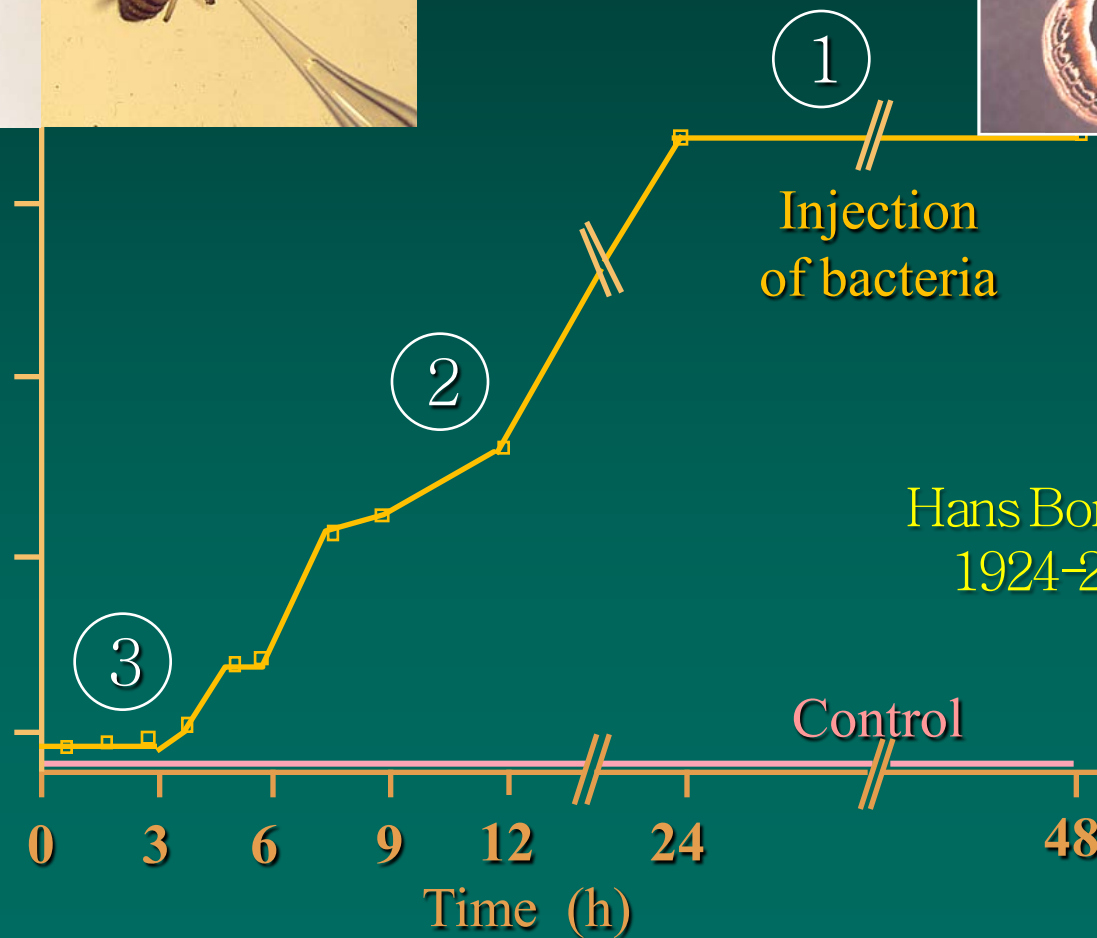


Hyalophora cecropia

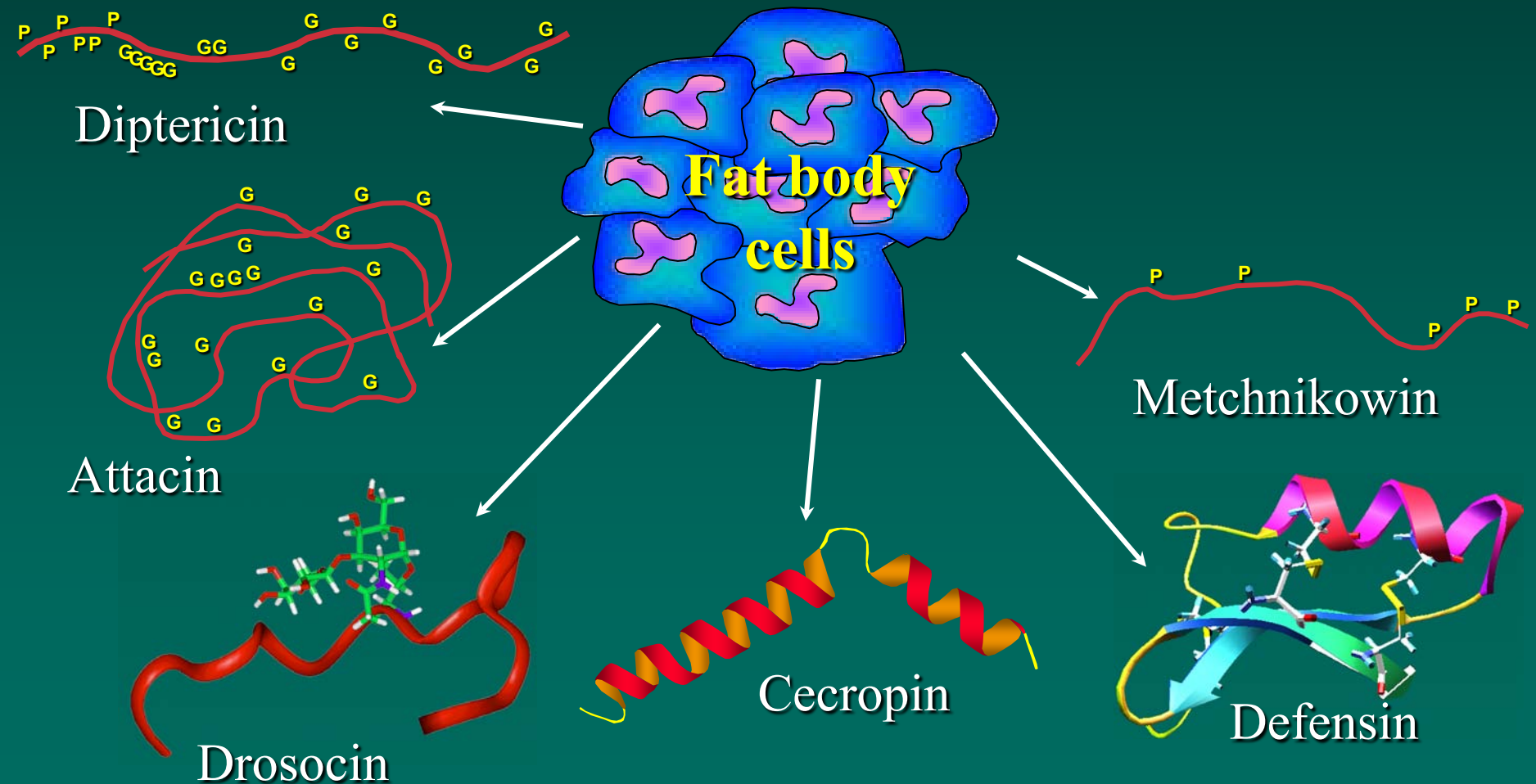


Hans Boman
1924-2008

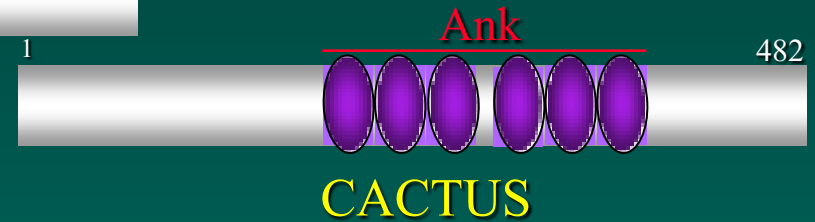
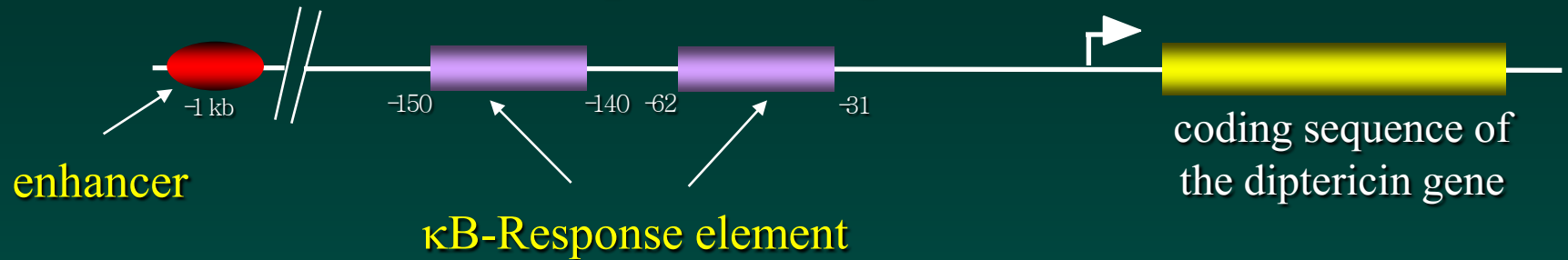
Antimicrobial activity in the cell-free hemolymph



Systemic (“humoral”) antimicrobial response in Drosophila – identification of antimicrobial peptides



NF- κ B response elements in the promoter of the dipteracin gene



Unchallenged

Diptericin-LacZ reporter gene

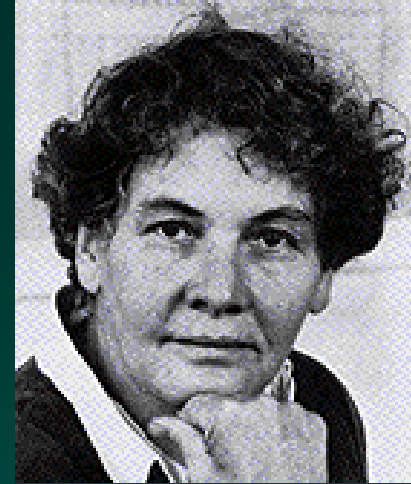


Challenged

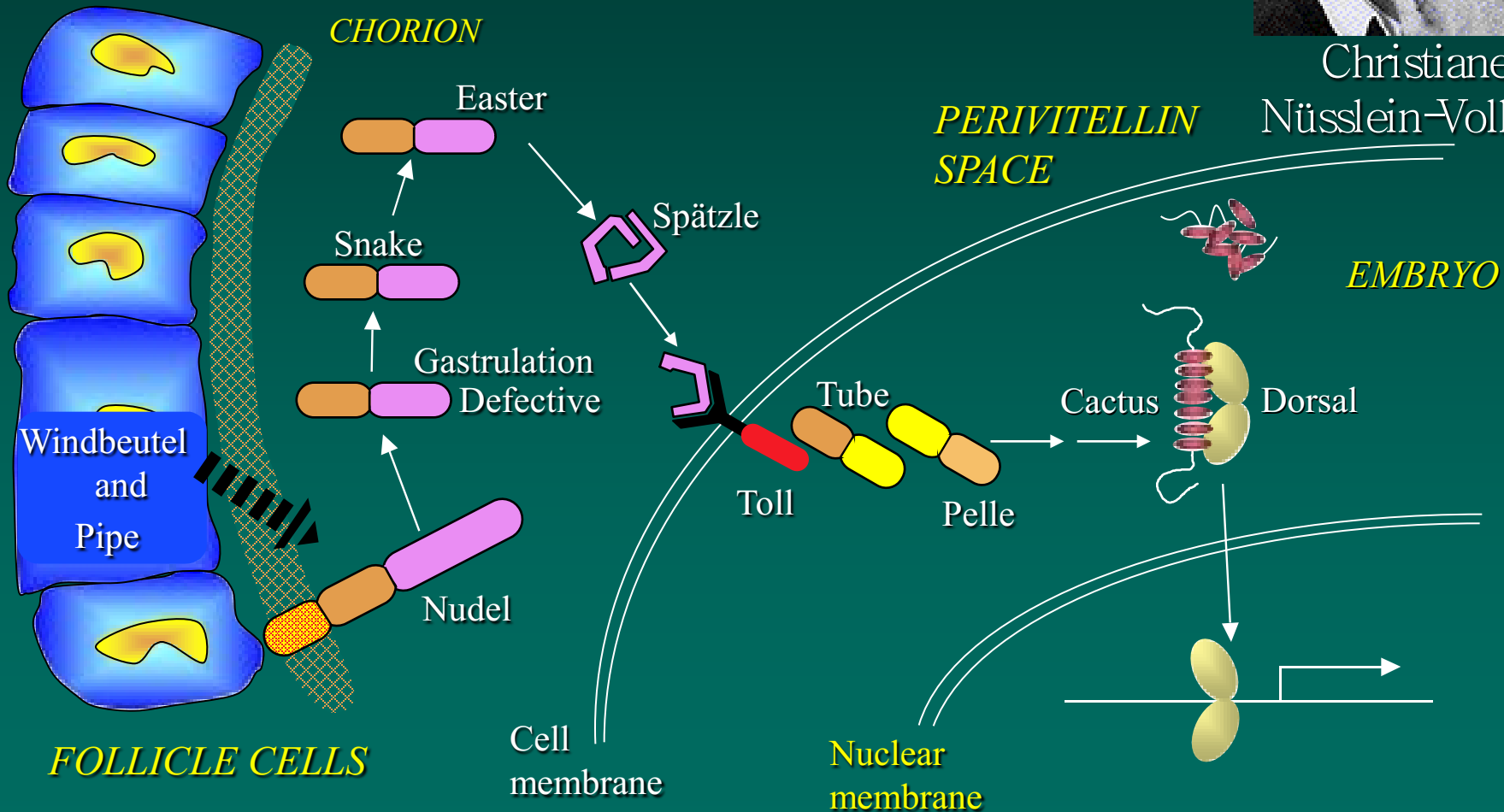
Versailles, 18 years ago, Innate Immunity Conference



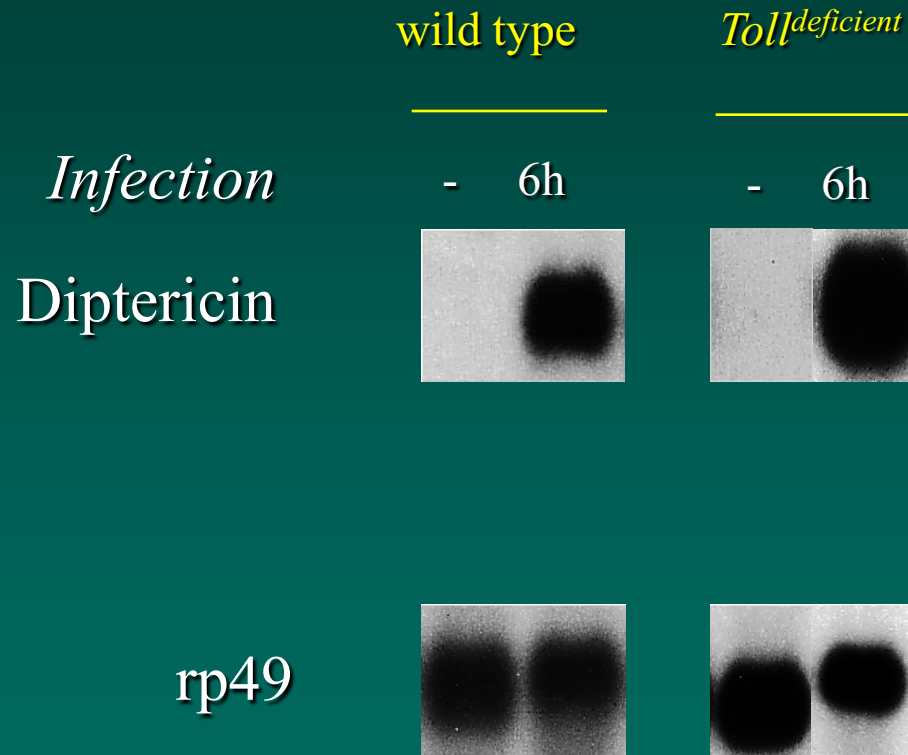
Gene cascade controlling the dorso-ventral axis in the *Drosophila* embryo

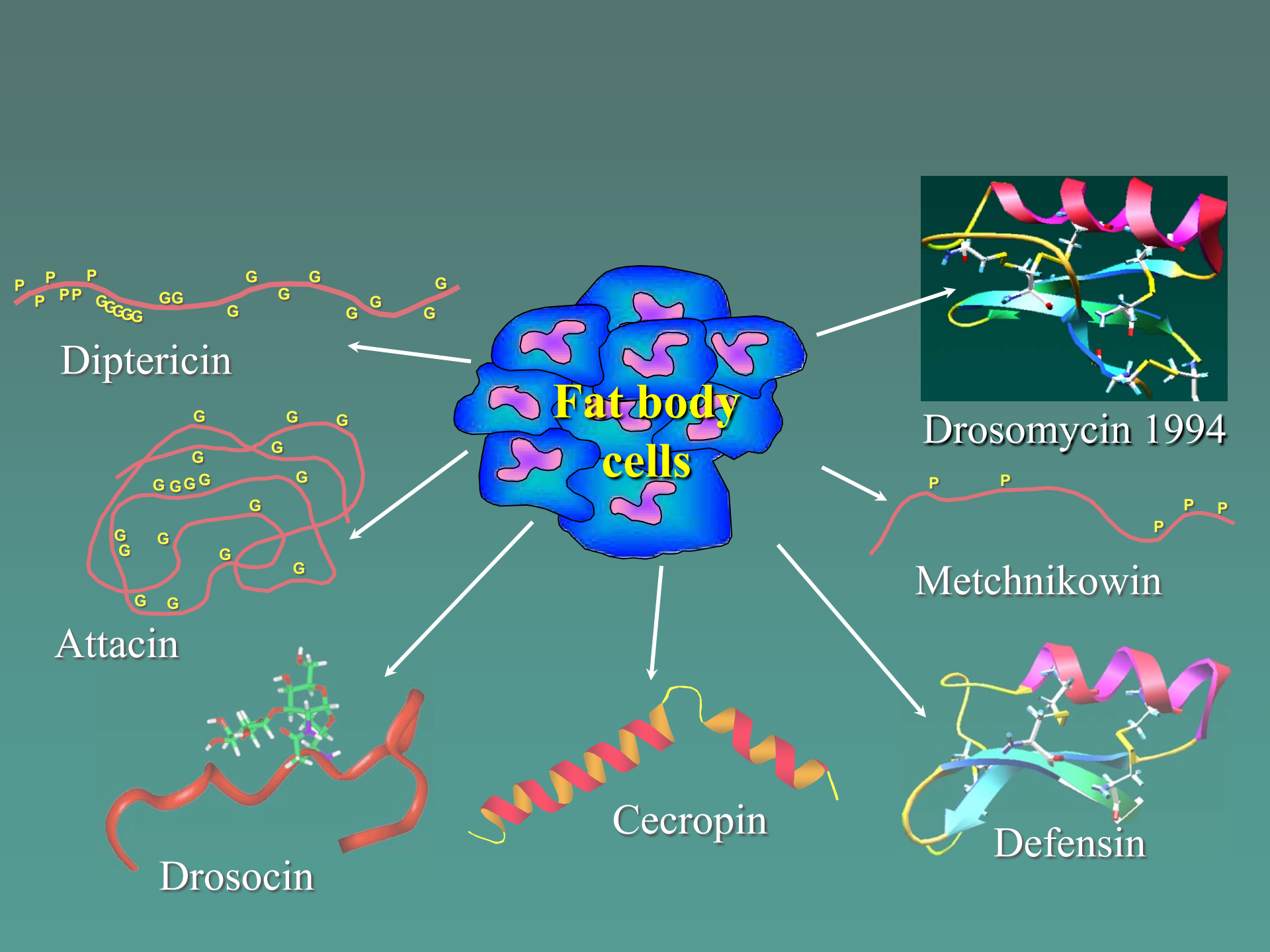


Christiane Nüsslein-Volhard

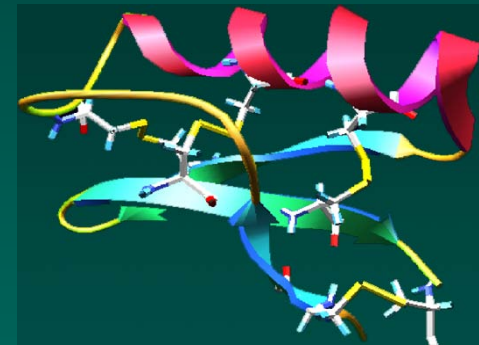
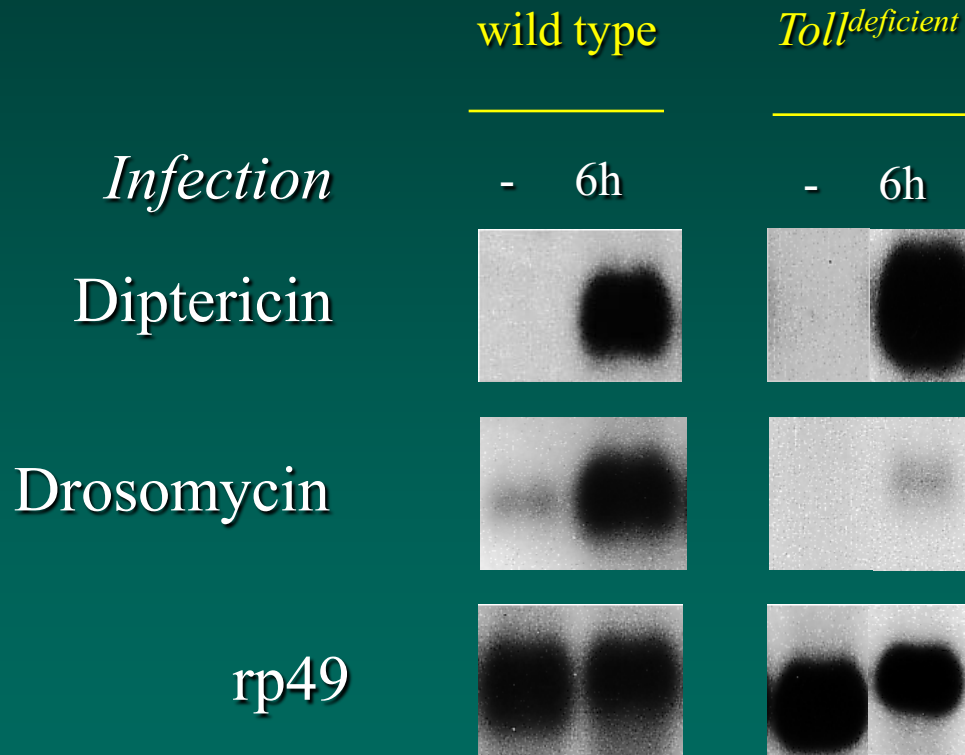


Do the genes of the Spätzle/Toll/Dorsal cassette control the challenge-induced expression of dipterincin ?



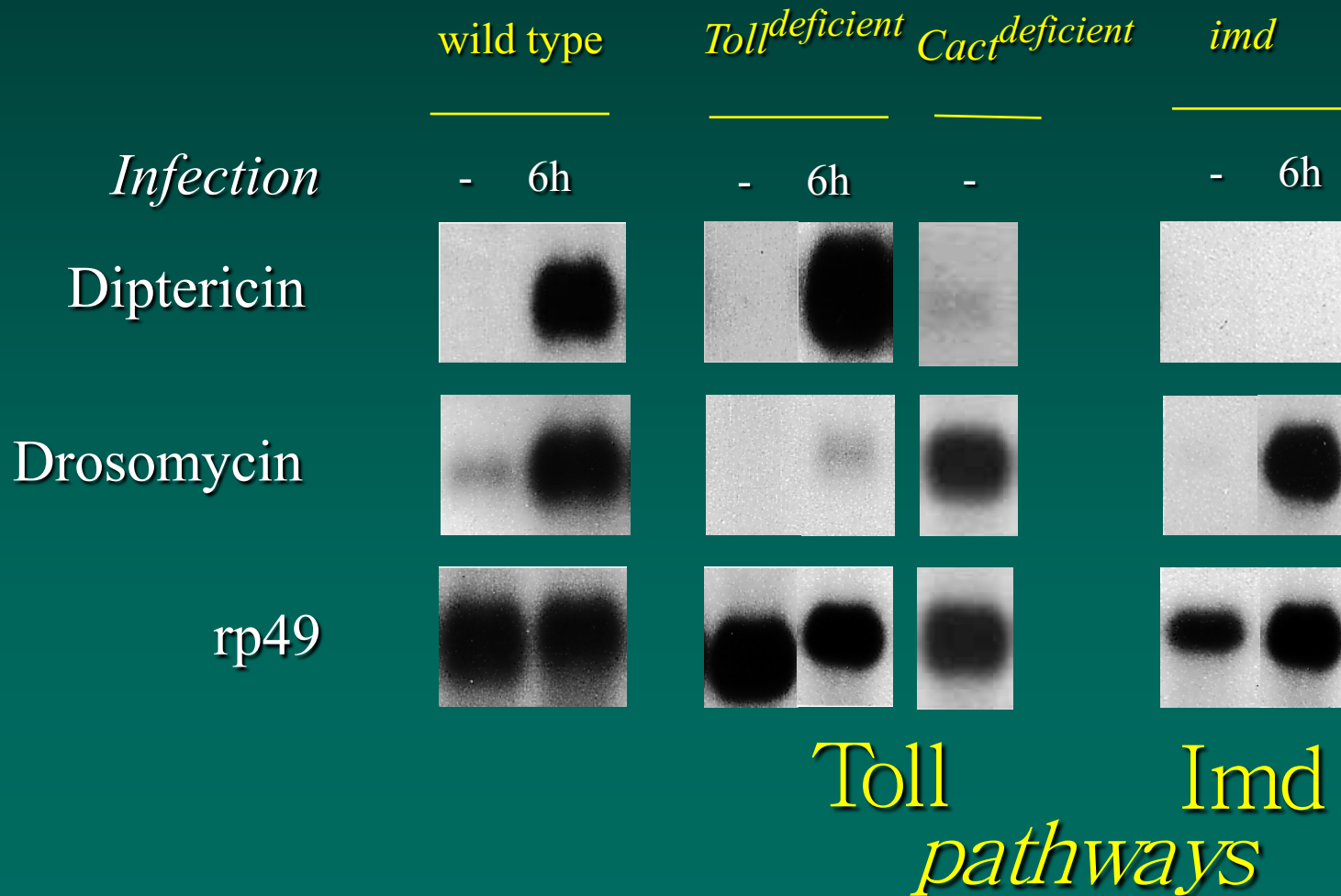


The challenge-induced expression of the Drosomycin gene is dependent on the Toll pathway.

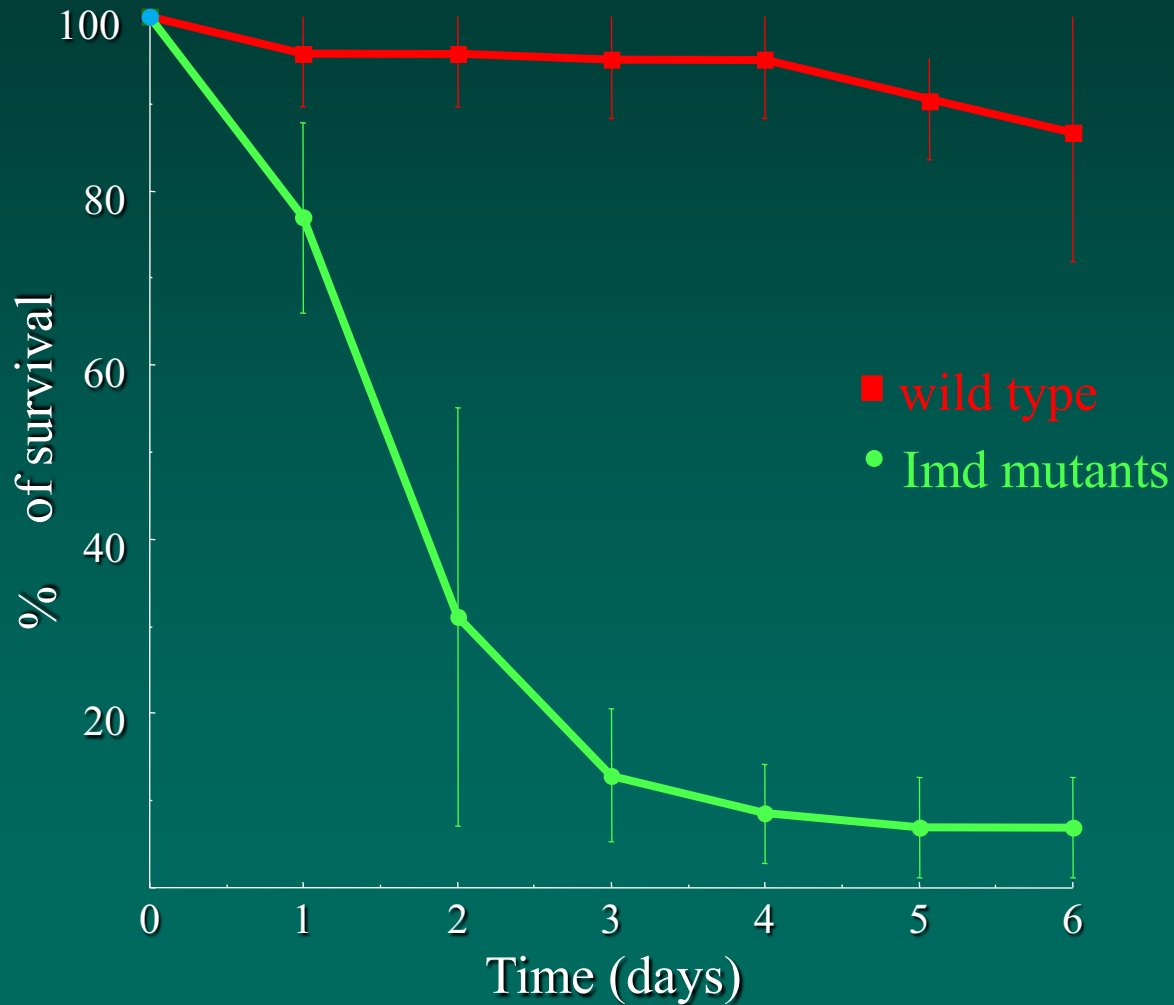


Drosomycin 1994

Two distinct pathways control the expression of antimicrobial peptides

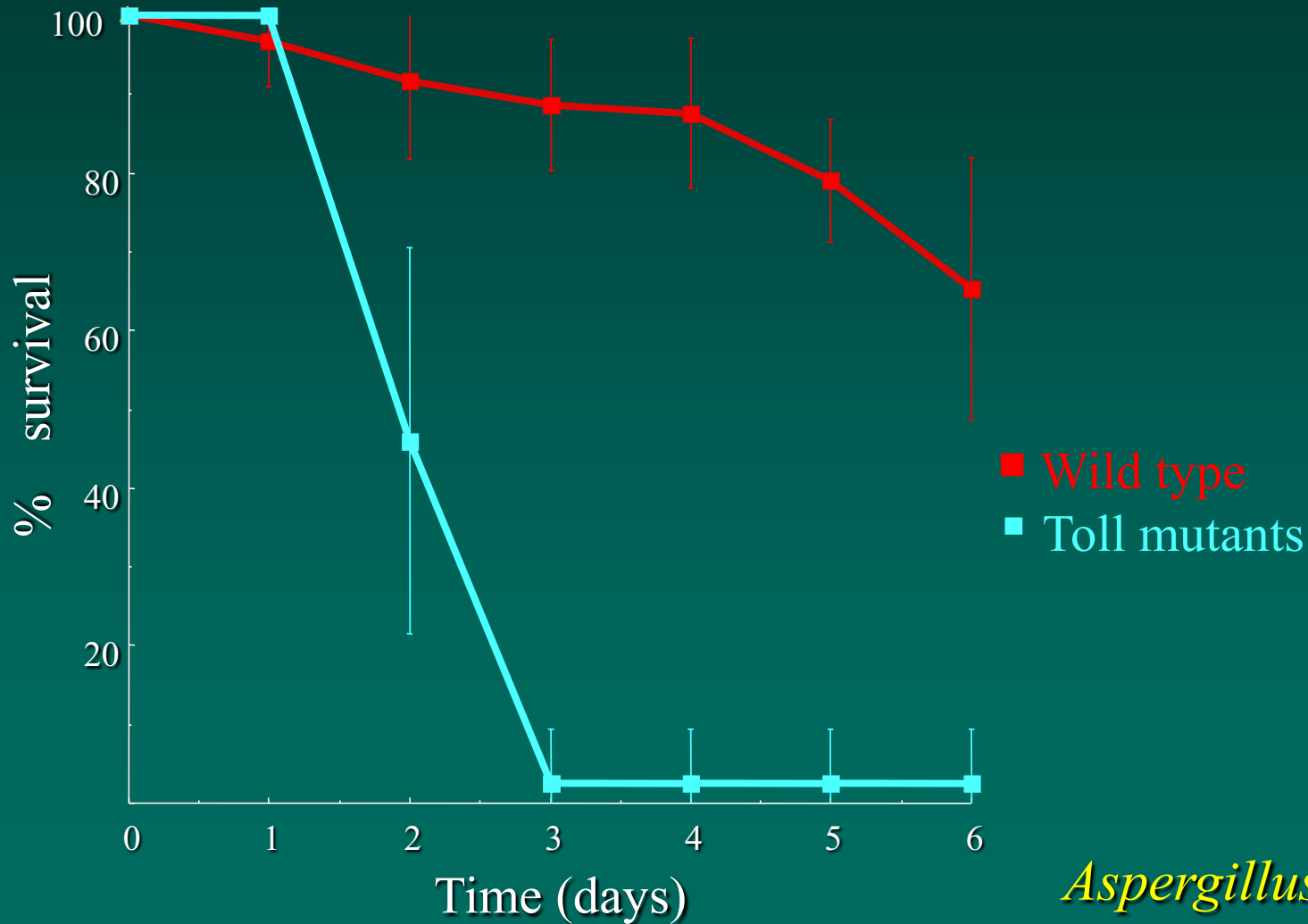


Imd pathway mutants are sensitive to bacterial infections

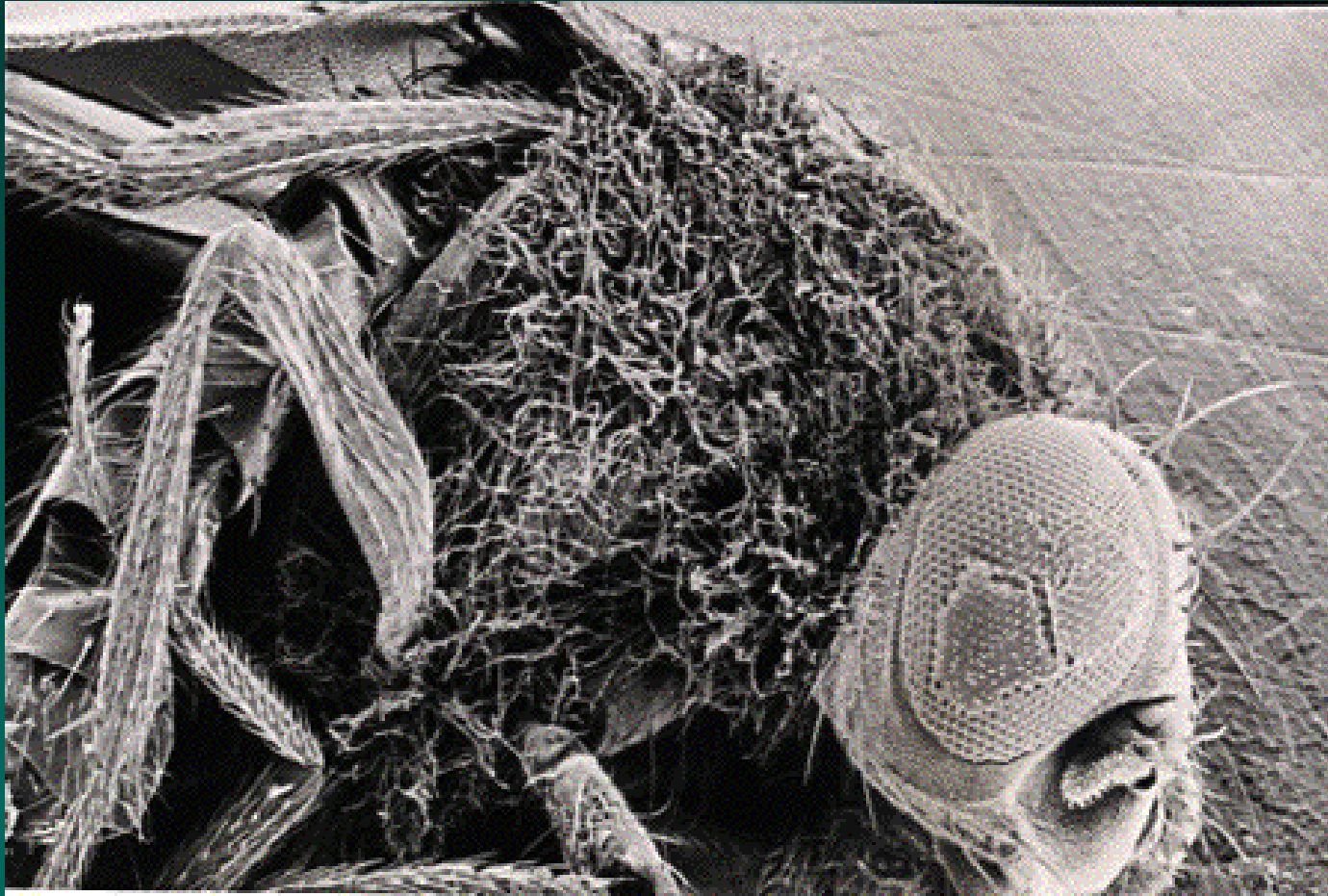


E. coli infection

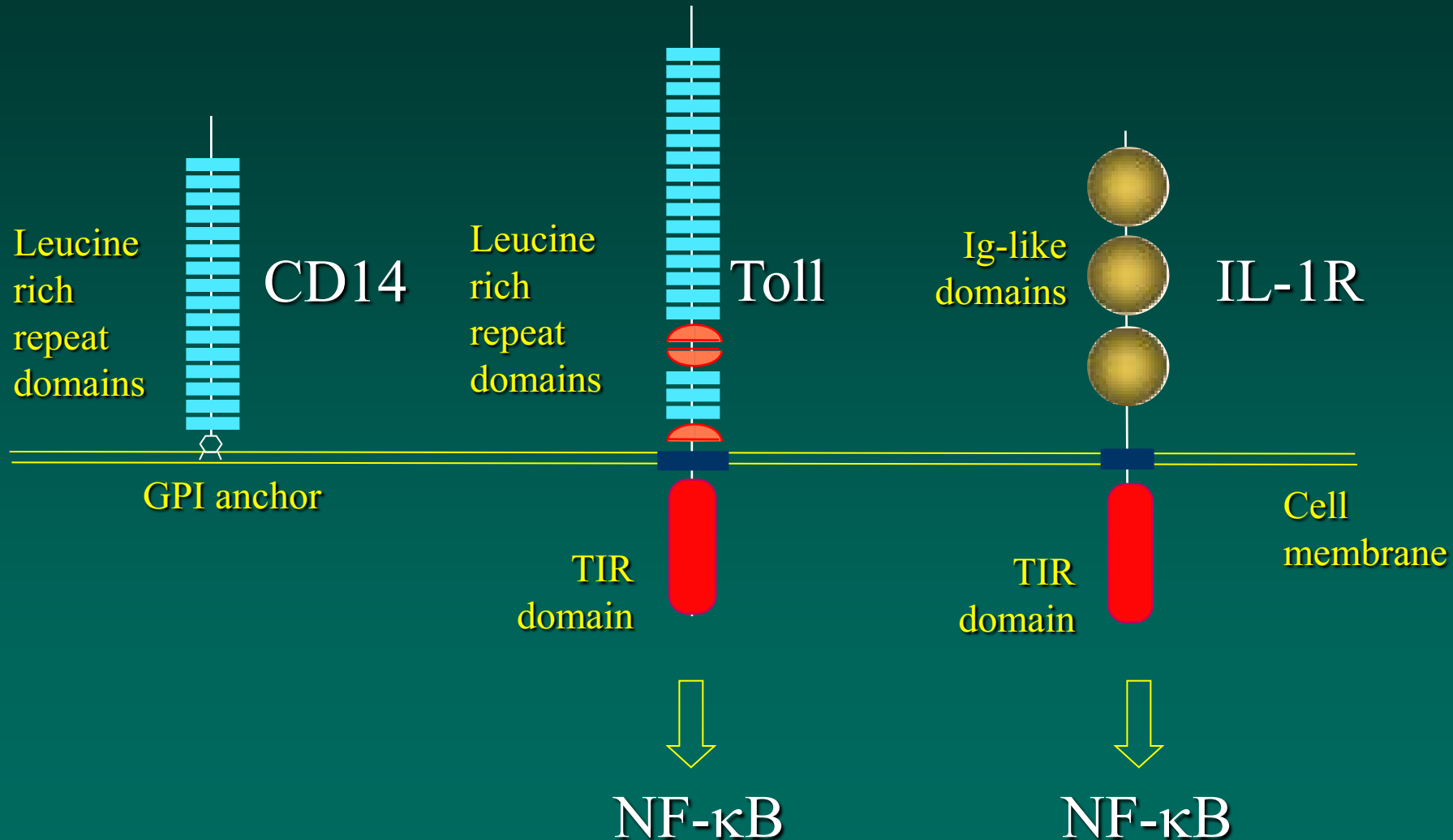
Toll pathway mutants are sensitive to fungal infections



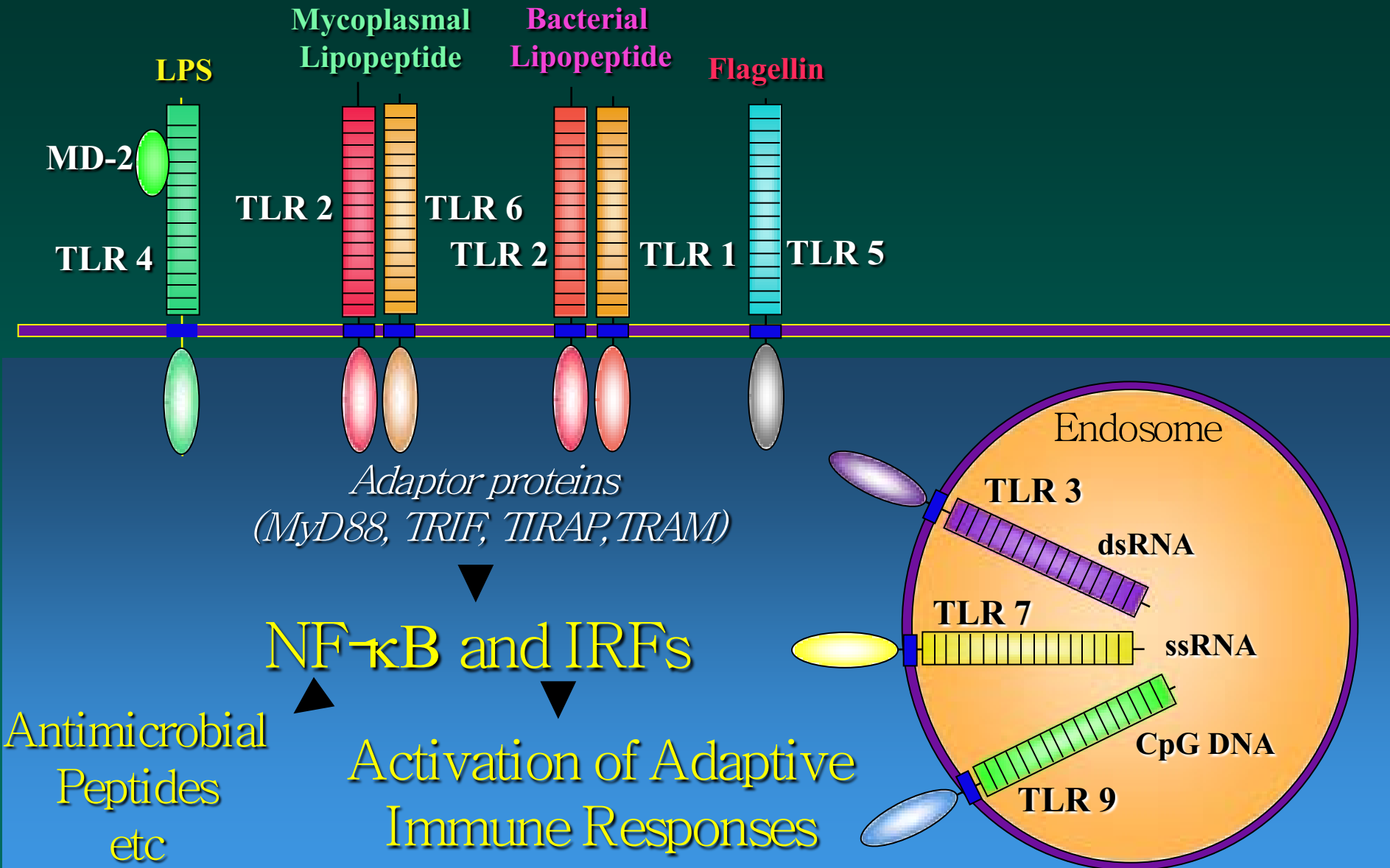
Overwhelming fungal infection in a Toll deficient background

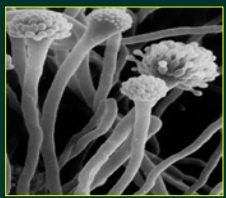


NF- κ B activation by Toll and IL-1

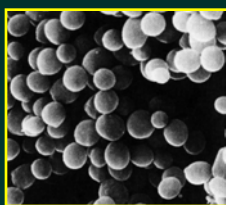


Activation of $NF-\kappa B$ by TLR family members





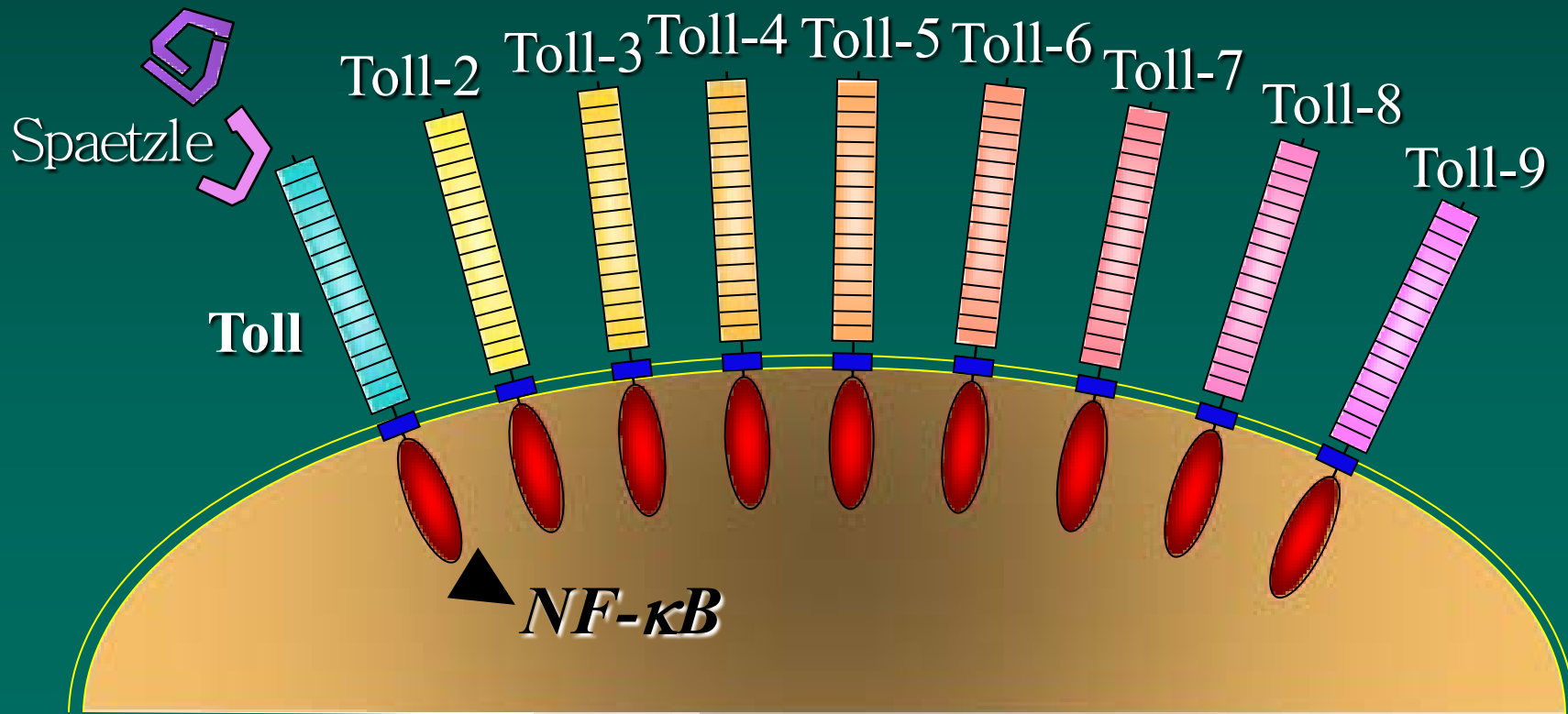
Fungi



Gram positive
bacteria

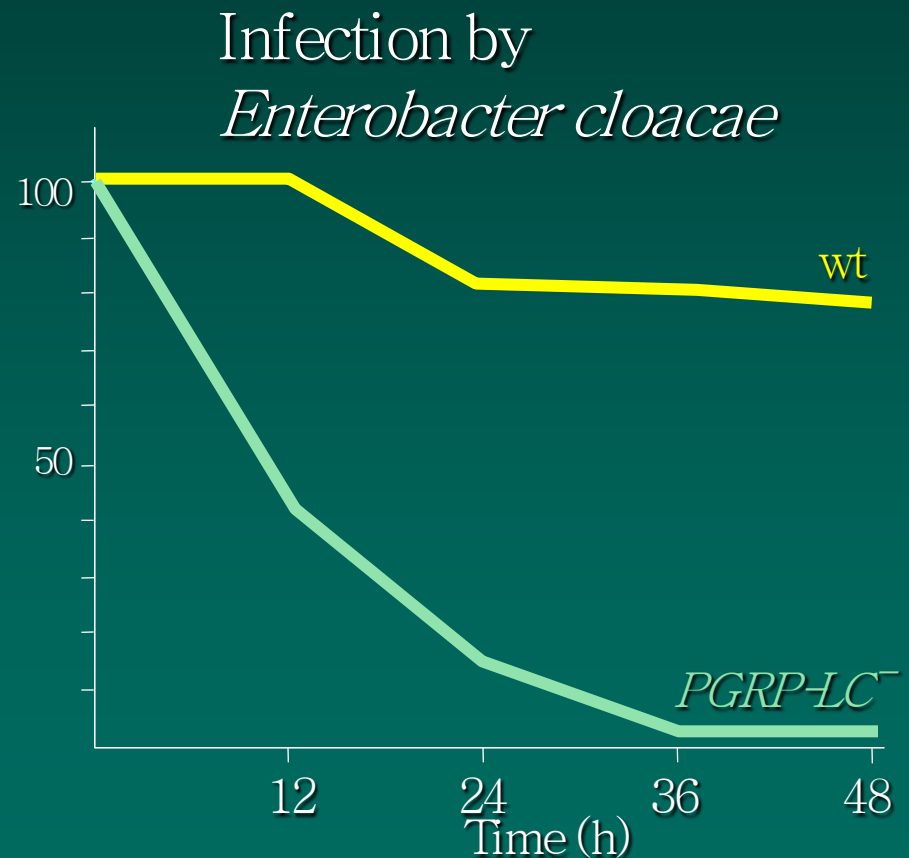
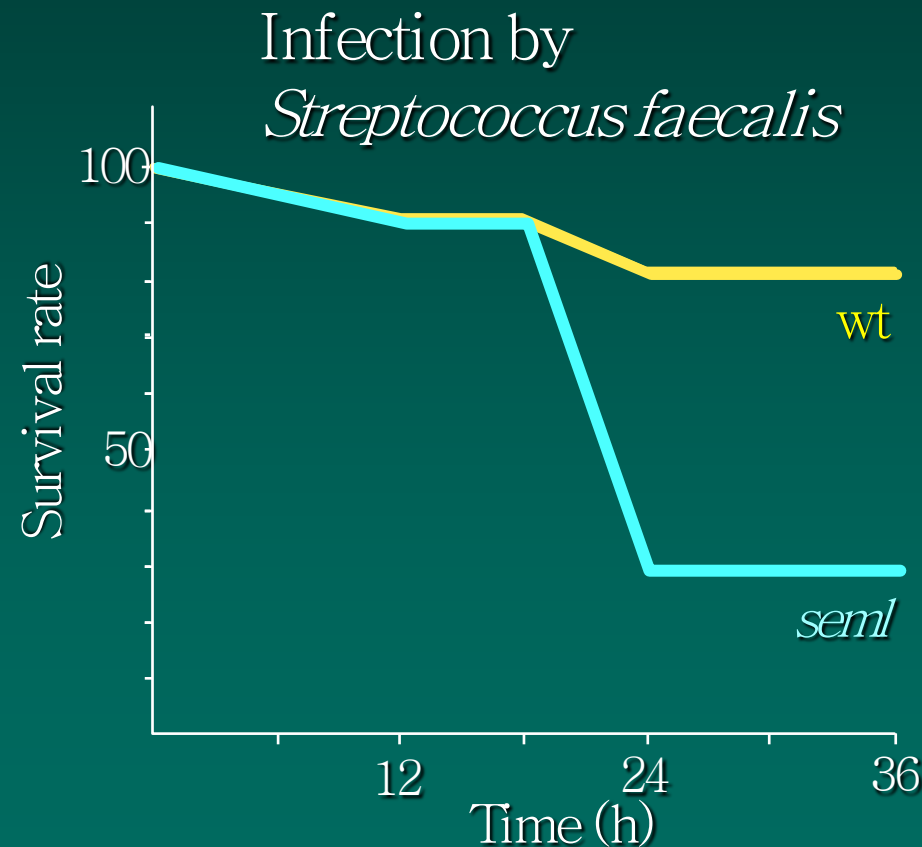
Receptors

Proteolytic
cascade



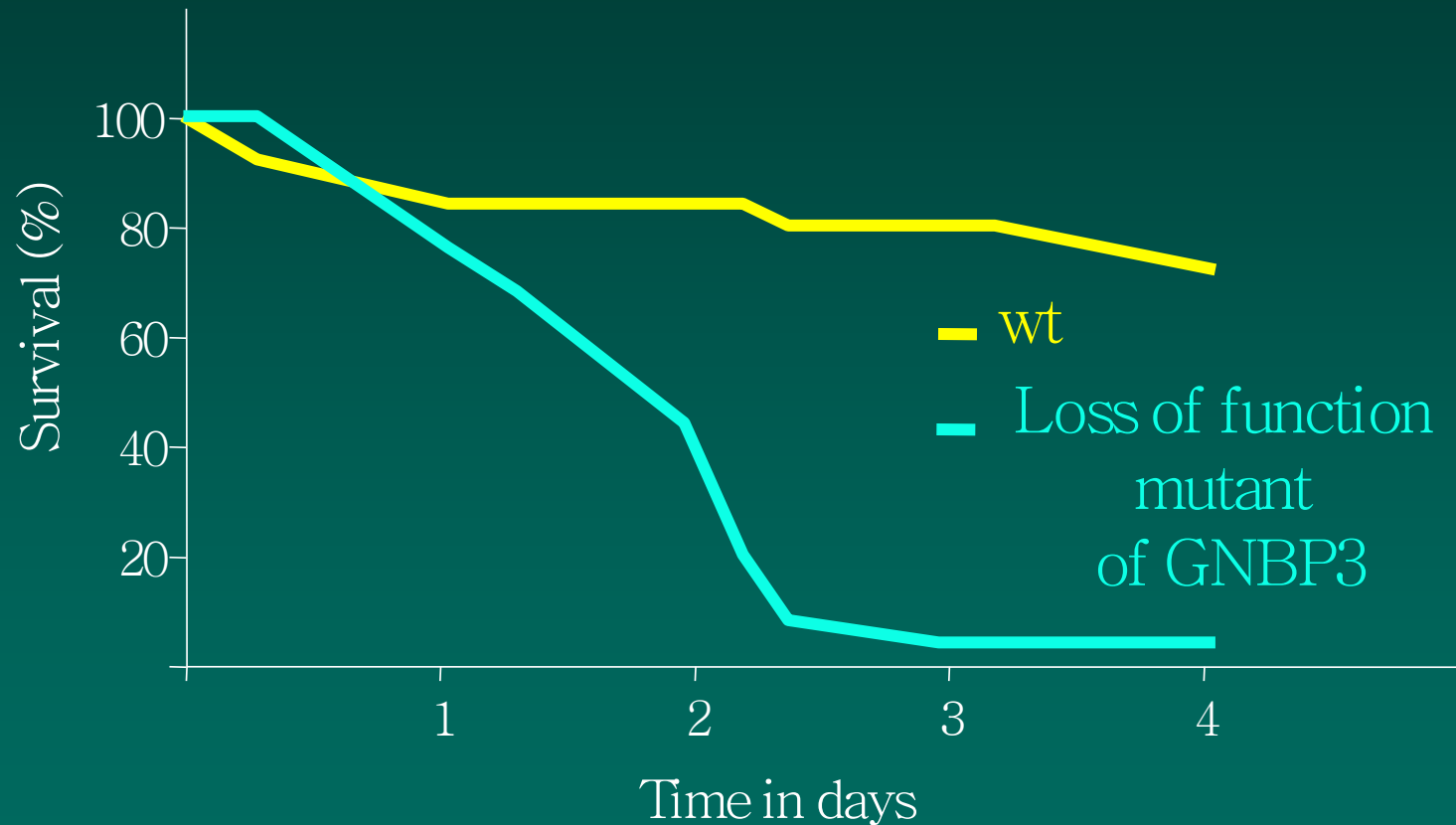
A mutation in the PGRP-SA gene (semmelweis) compromises the anti-Gram-positive defense

A mutation in the PGRP-LC gene compromises the defense against Gram-negative bacteria



Royet and coll. 2001, Royet, Ferrandon and coll., Anderson and coll., Ezekowitz and coll. 2002

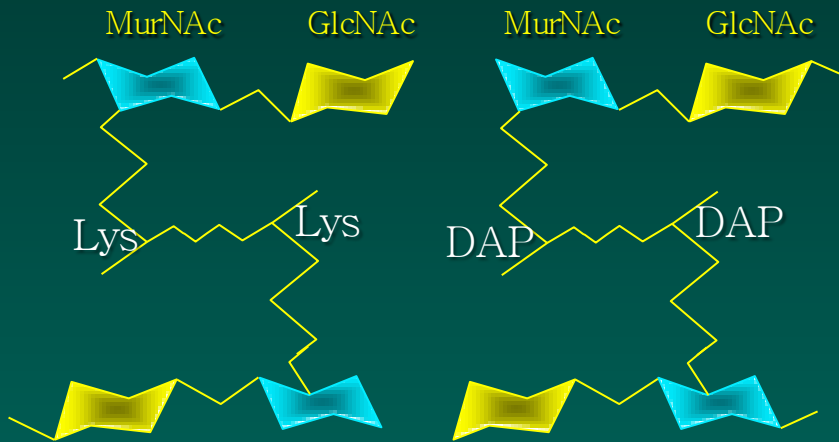
A mutation in the gene encoding GGBP3
compromises resistance to Candida infections



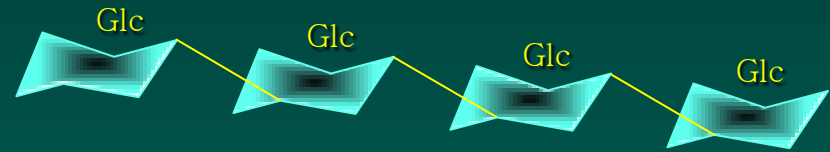
Microbial Inducers of Immune Responses and Cognate Receptors in Flies:

Peptidoglycan Recognition Proteins and Glucan Binding Proteins

Peptidoglycan



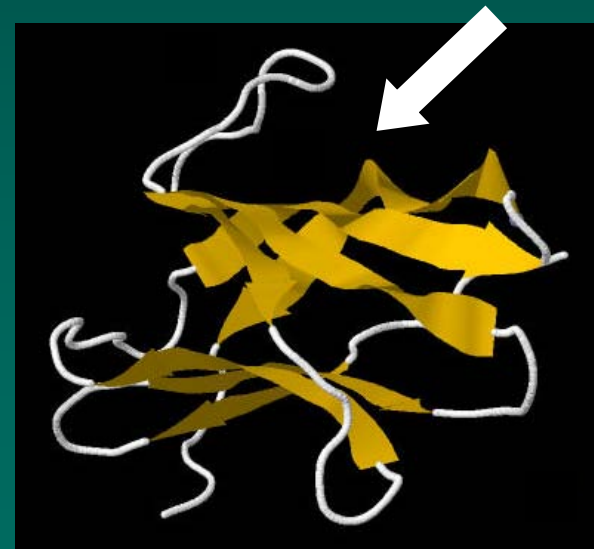
β -(1,3)-Glucan



PGRP

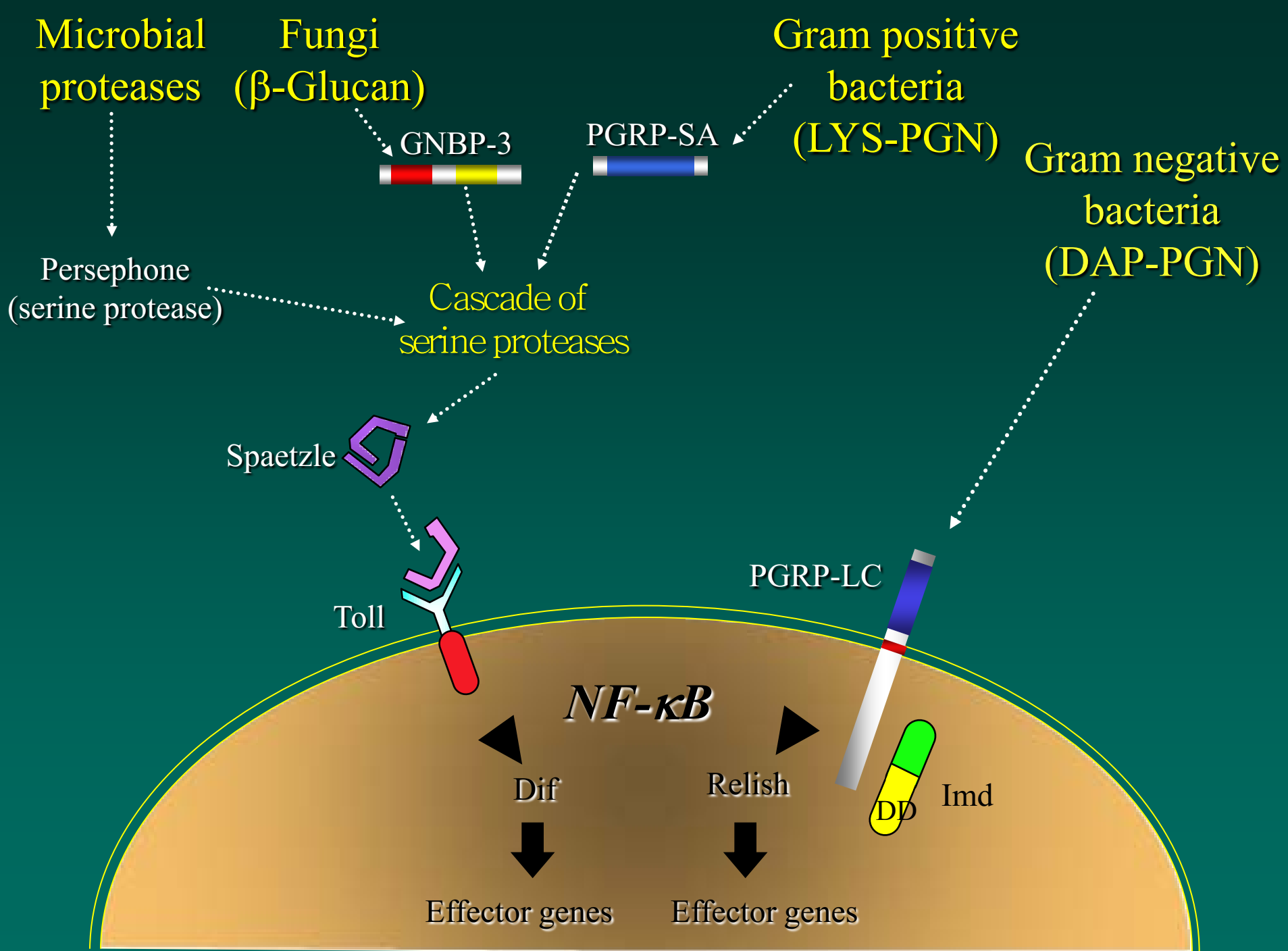


GNBP

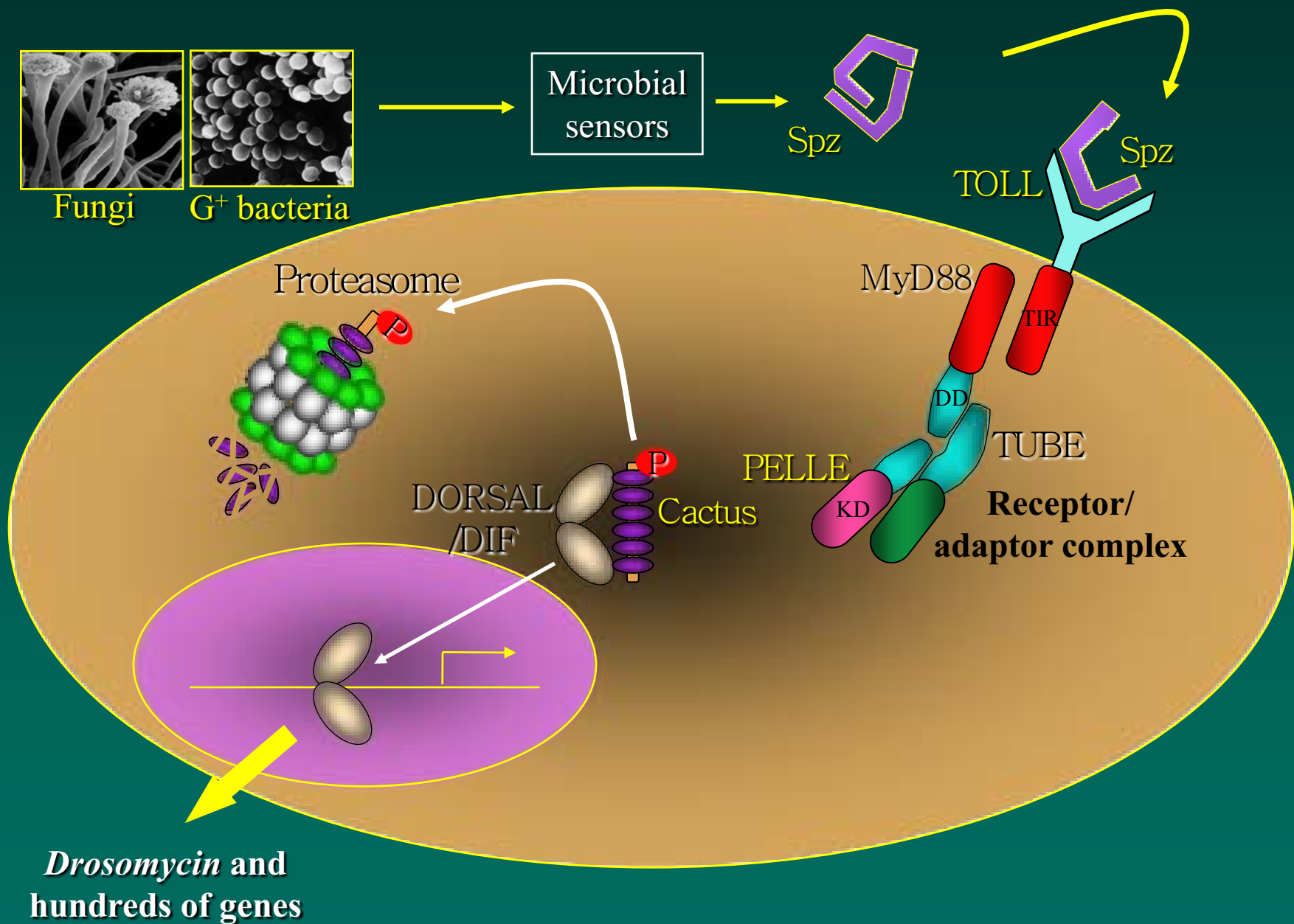


Rousse/ and coll.

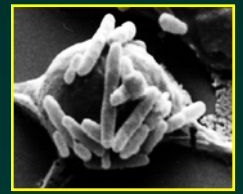
Werner and coll.; Kim and coll.; Reiser and coll.; Chang and coll.



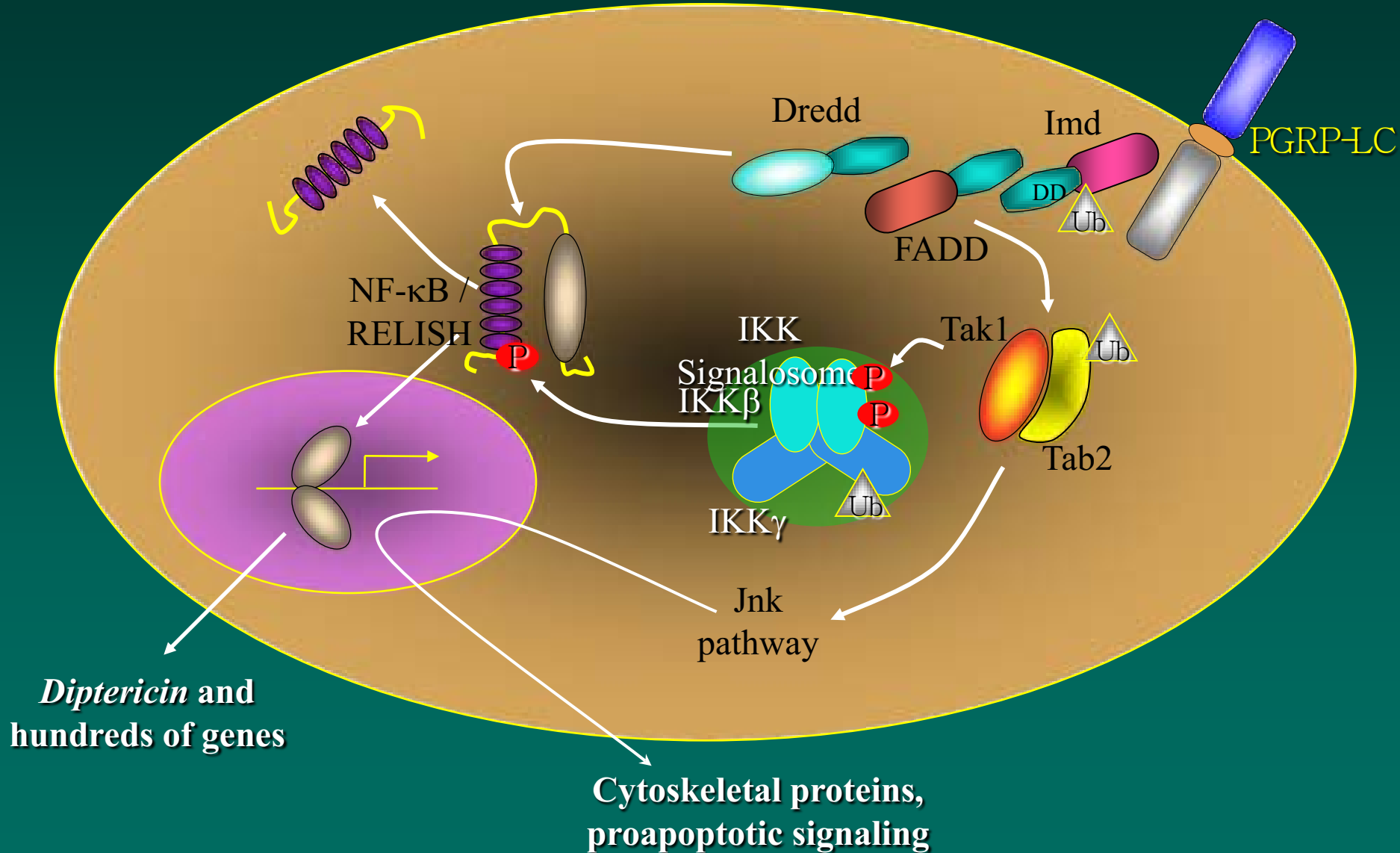
NF- κ B activation by Toll in Drosophila

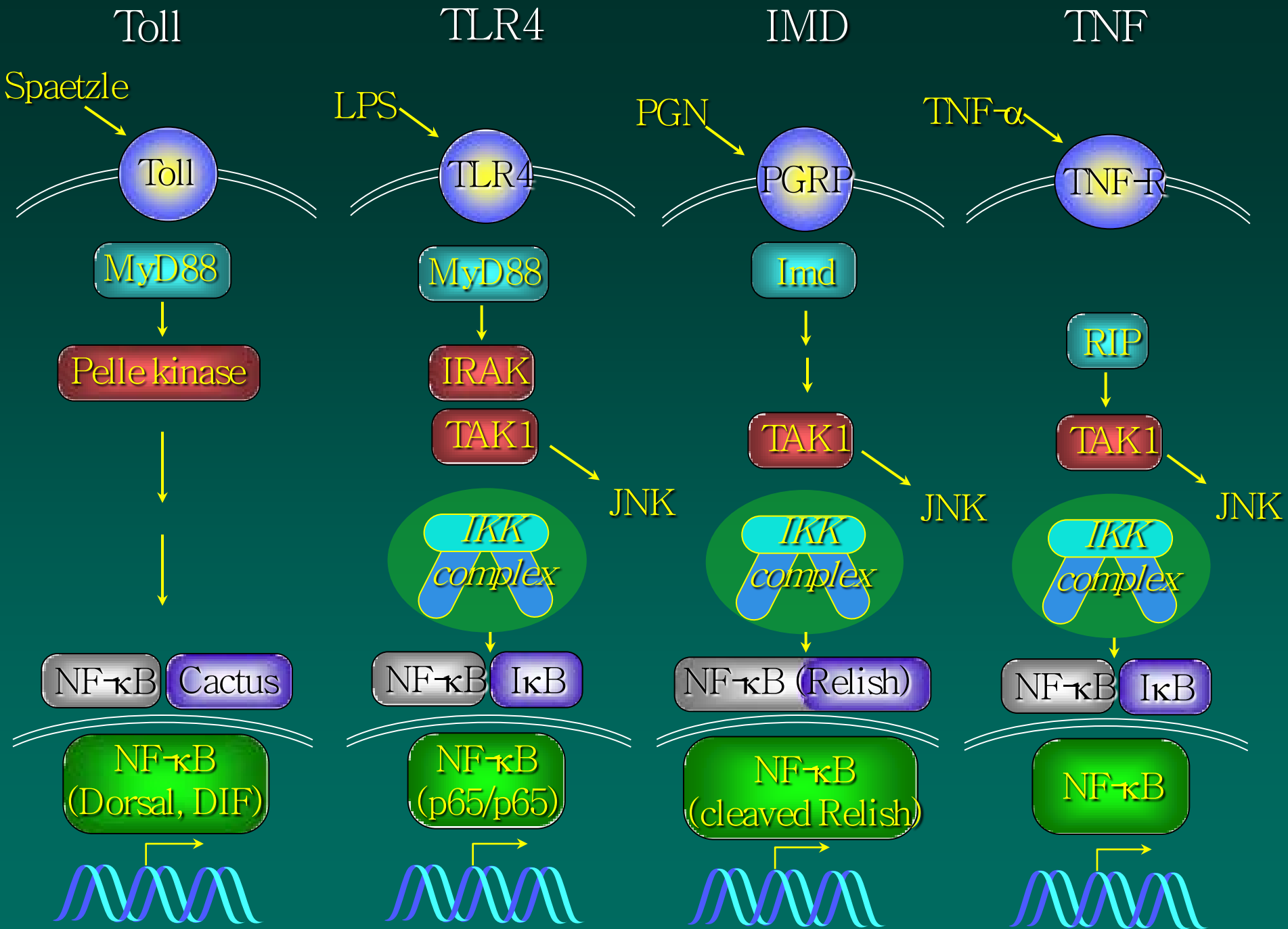


NF-κB activation by *IMD* in *Drosophila*



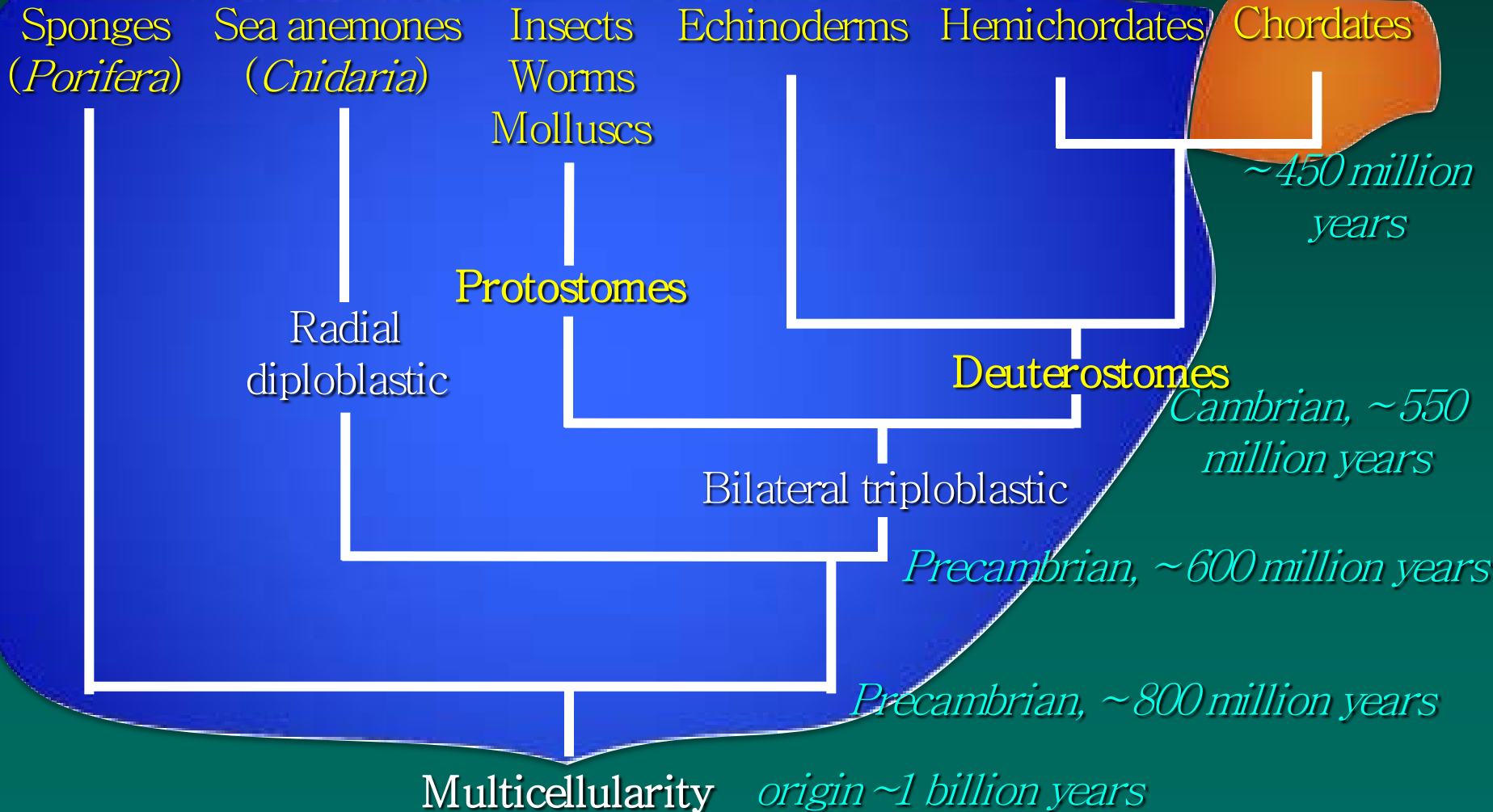
G- Bacteria





Phylogeny of Innate Immune Defenses

AMP	AMP	AMP	AMP	AMP	AMP
NF- κ B	NF- κ B	NF- κ B	NF- κ B	NF- κ B	NF- κ B
TAK1	TAK1	TAK1	TAK1	TAK1	TAK1
TOLL	TOLL	TOLL	TOLL	TOLL	TOLL



Acknowledgements



D. Hoffmann



C. Hetru



J.L. Dimarcq



J.M. Reichhart



B. Lemaitre



D. Ferrandon



J. Royet



J.L. Imler



E. Levashina



M. Lagueux



P. Bulet

Credits : Drosophila immunity

USA,

Kathryn Anderson

Carl Hashimoto

Steve Wasserman

Tony Ip

Ruth Stewart

Shuba Govind

Neal Silverman

Tom Maniatis

Alan Ezekowitz

Nathalie Franc

Linda Stuart

Christine Kocks

Norbert Perrimon

Herve Agaisse

Michael Boutros

David Schneider

Europe,

Hans Boman†

Hakan Steiner

Dan Hultmark

Ingrid Faye

Ylva Engström

Ulli Theopold

Bruno Lemaitre

François Leulier

Julien Royet

Mika Ramet

Nick Gay

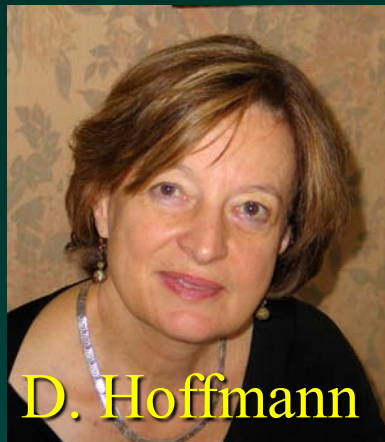
Asia,

Shoichiro Kurata

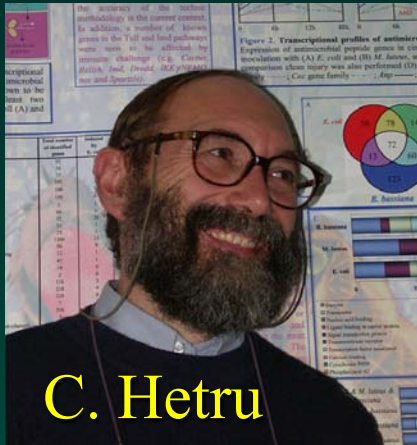
Won-Jae Lee

Young-Joon Kim

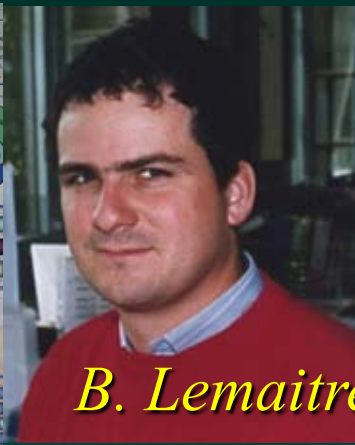
Acknowledgements



D. Hoffmann



C. Hetru



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J.L. Dimarcq



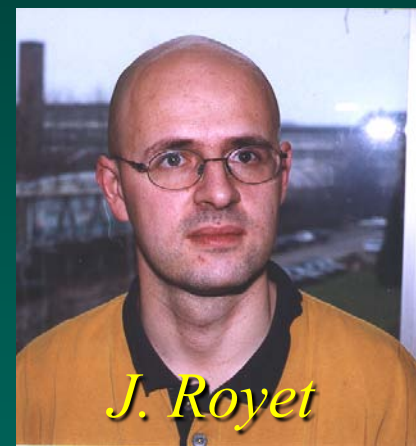
J.M. Reichhart



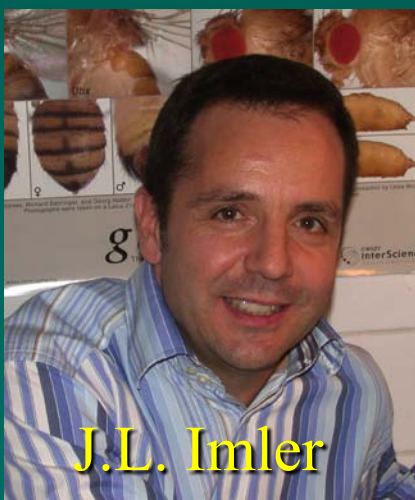
D. Ferrandon



M. Meister



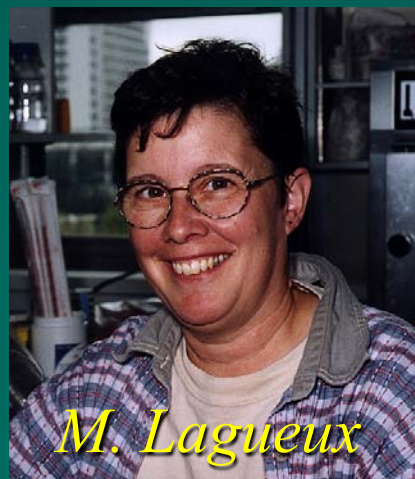
J. Royet



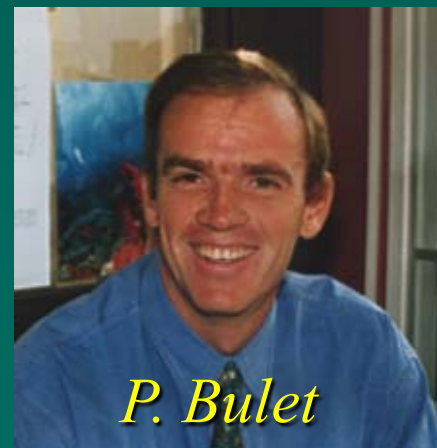
J.L. Imler



E. Levashina



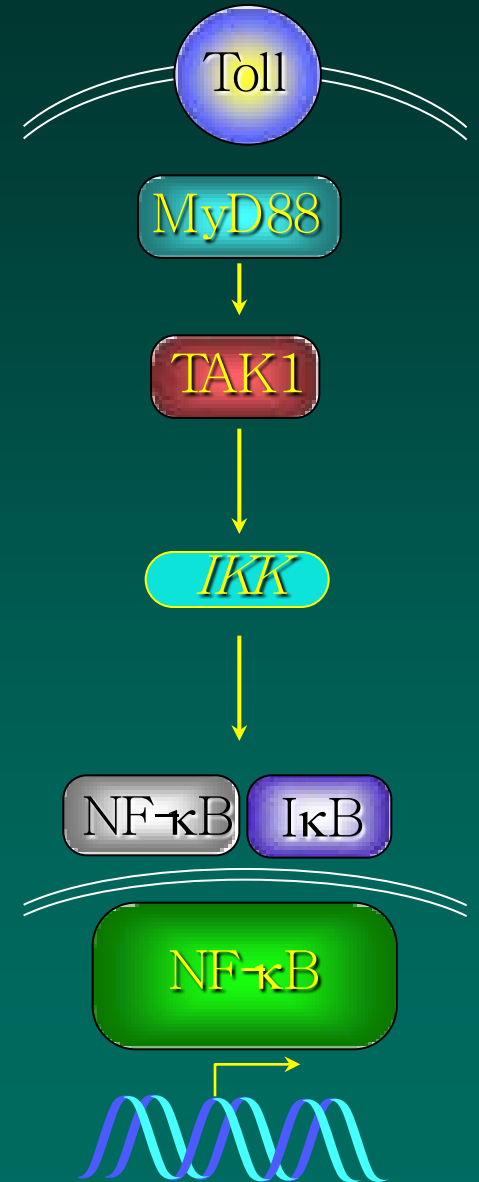
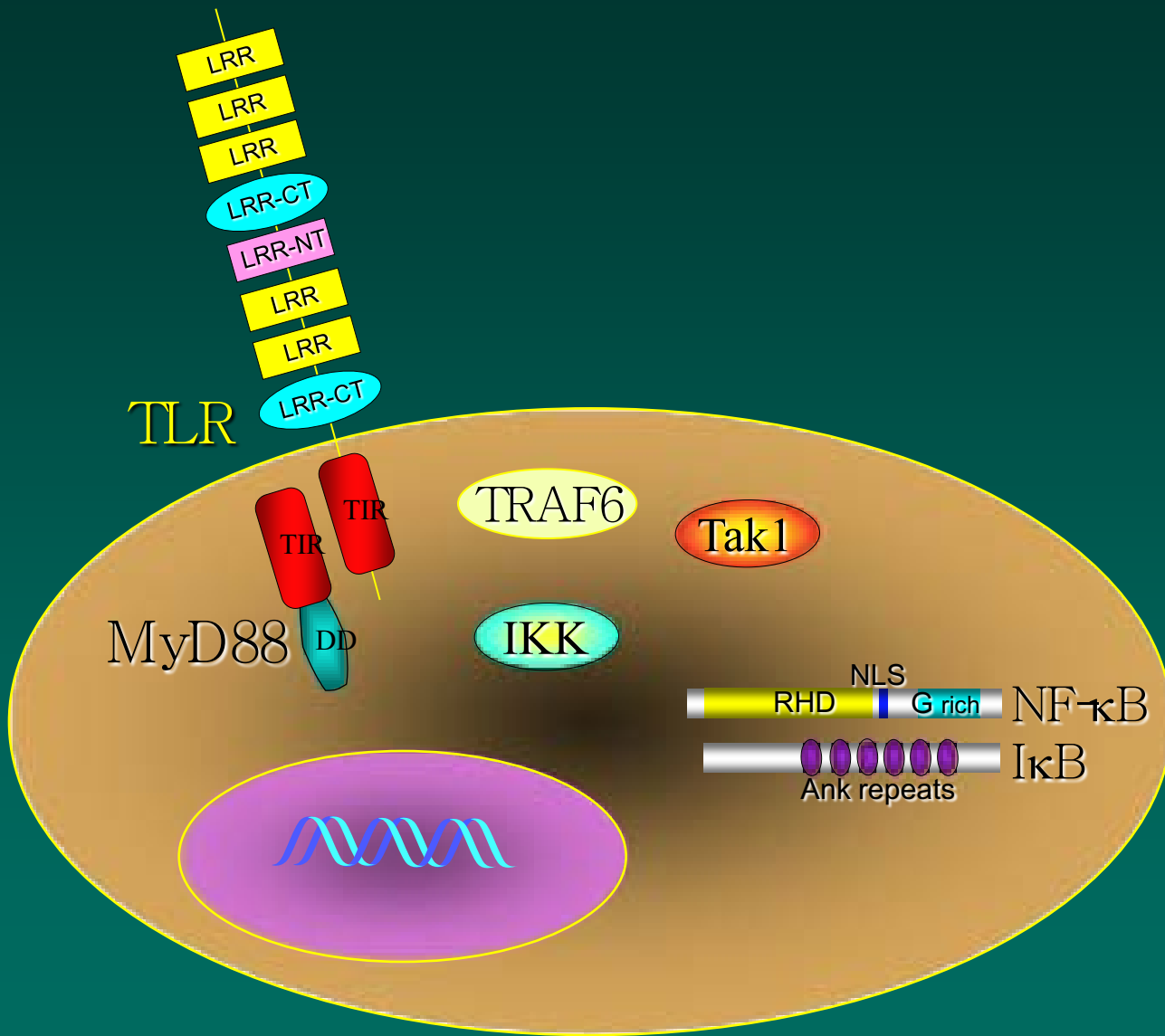
M. Lagueux

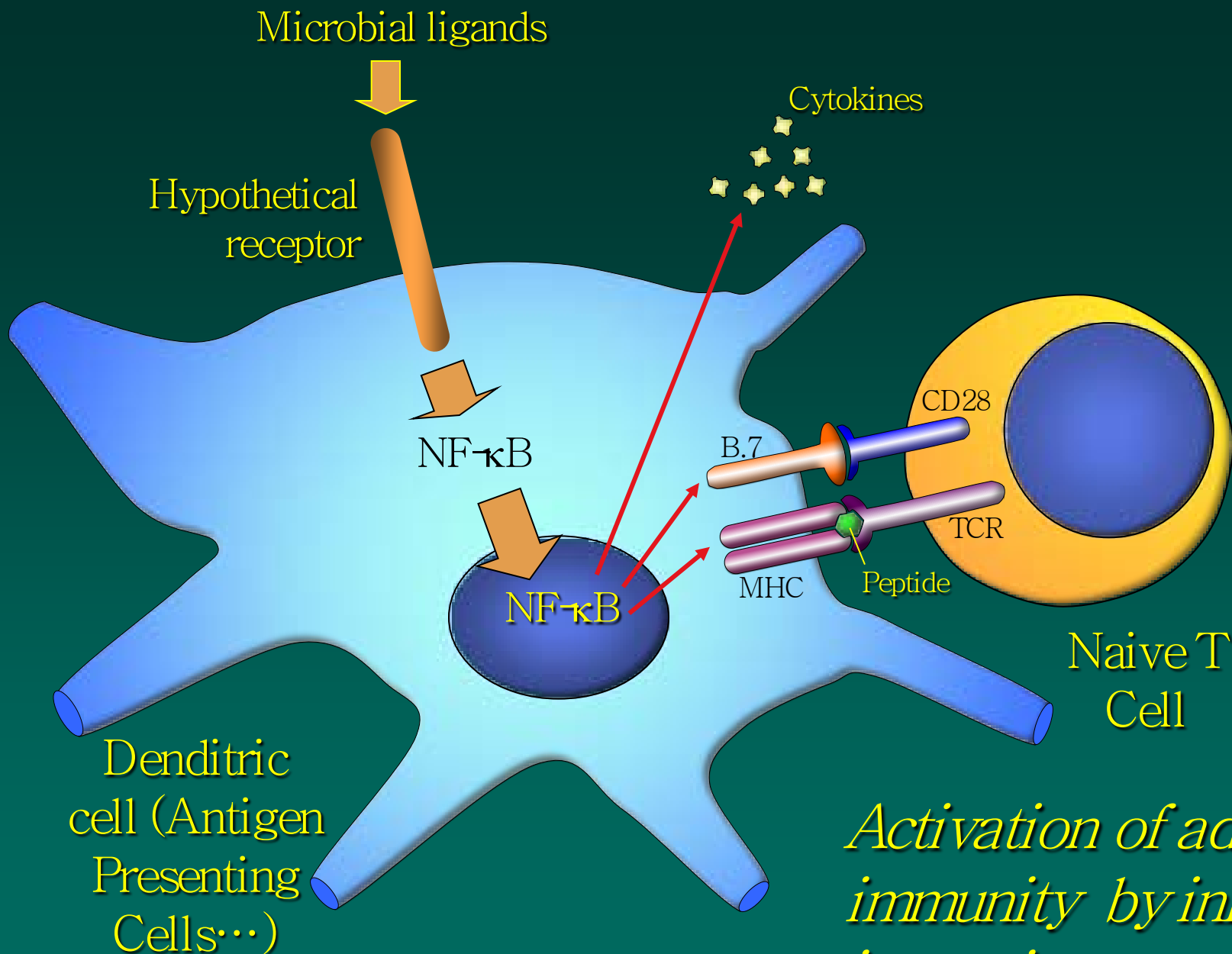


P. Bulet

The sea anemone *Nematostella*

Nematostella





Activation of adaptive immunity by innate immunity