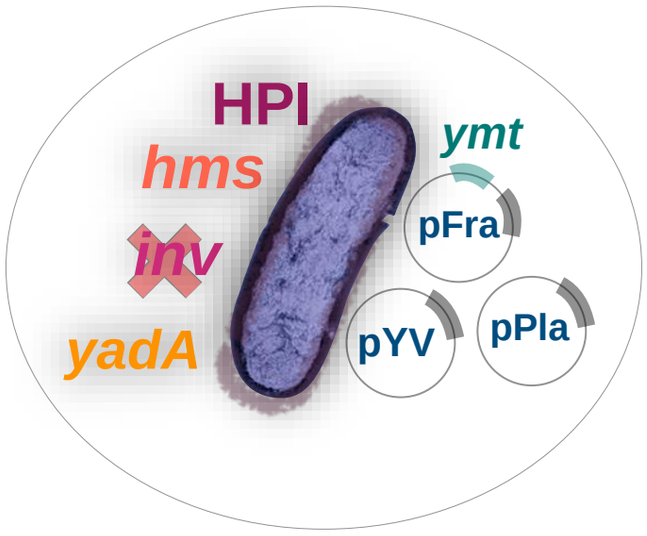
Pathogen X
August 29th-30th, 2022

Bacterial evolution & Plague



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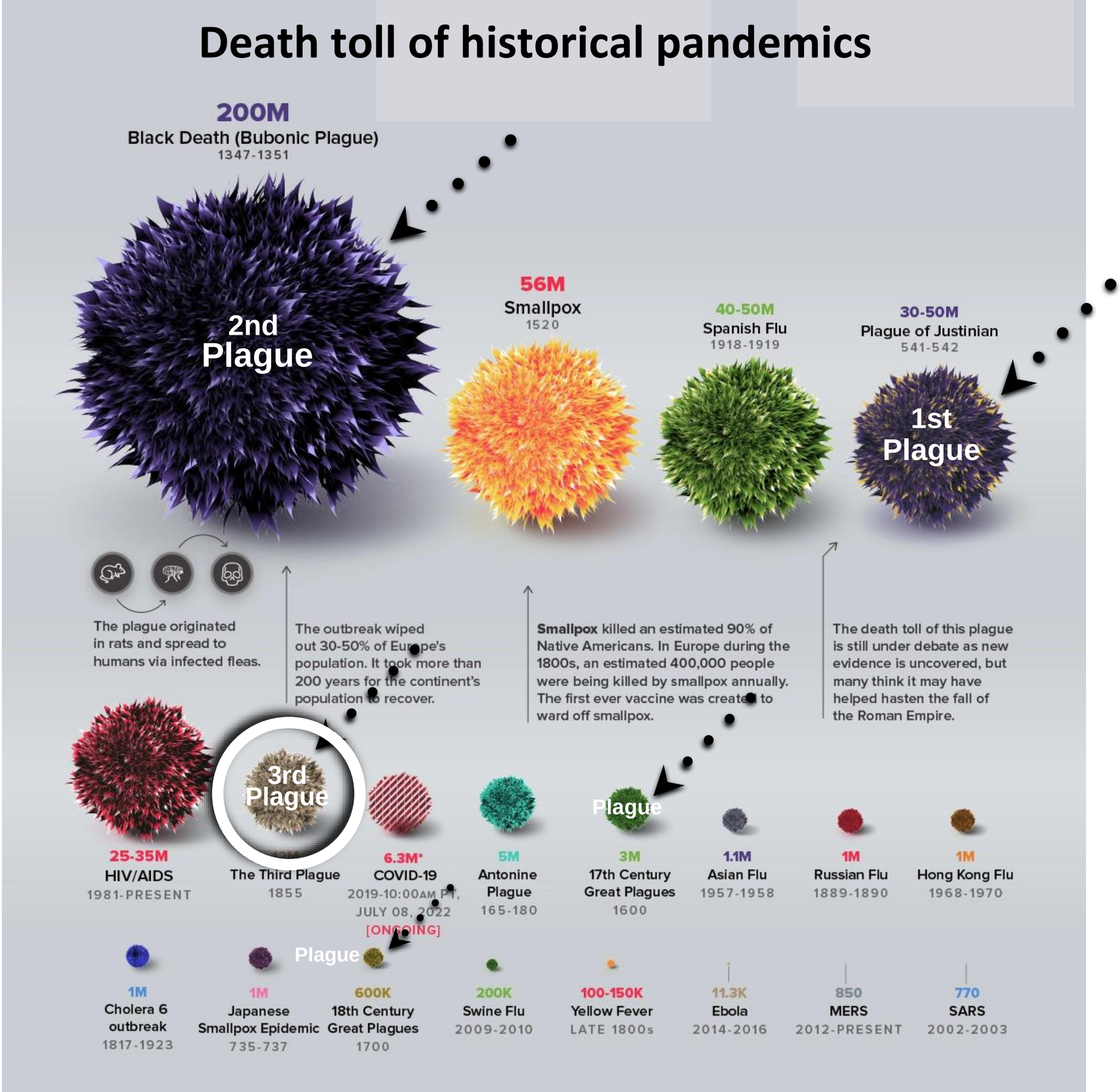
World Health Organization
Collaborating Centre for Plague (FRA-140)

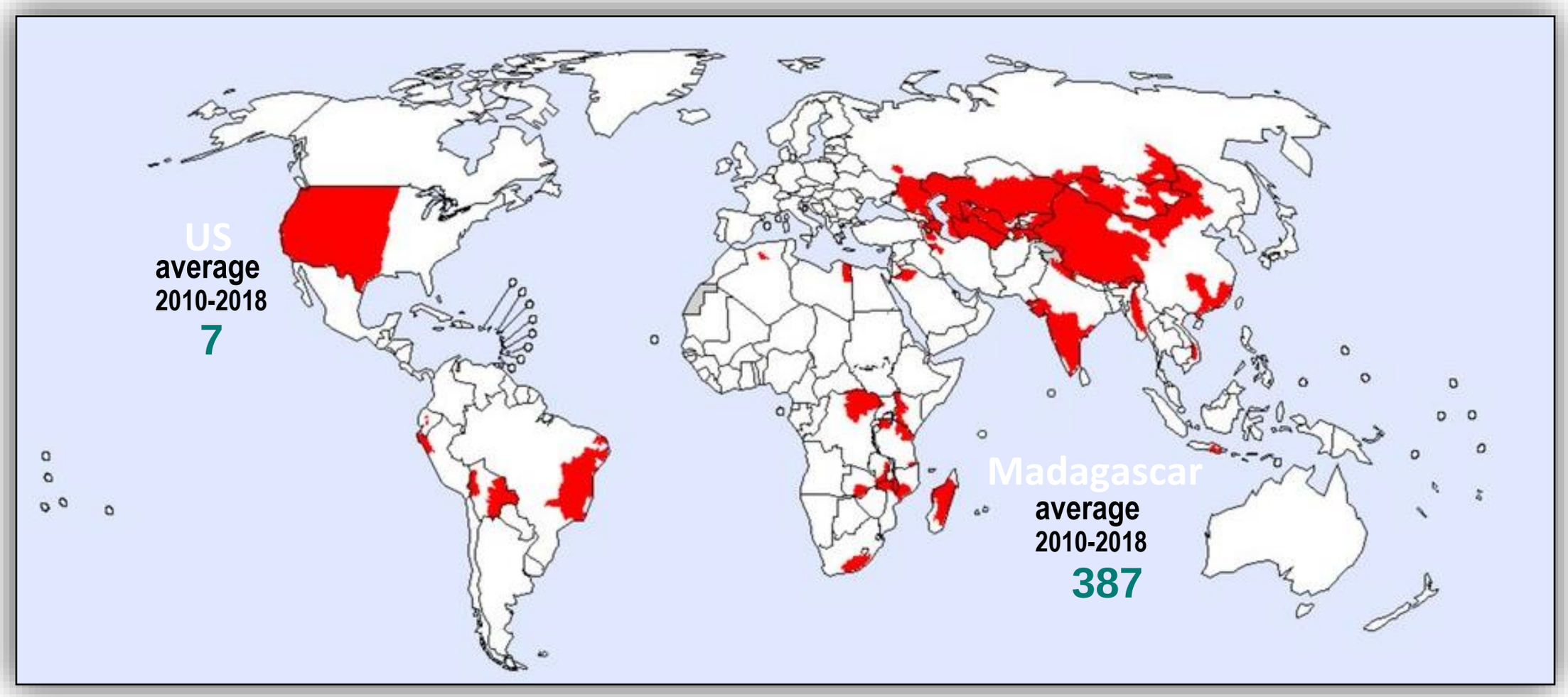
NATIONAL REFERENCE LABORATORY
Plague & Other Yersinioses

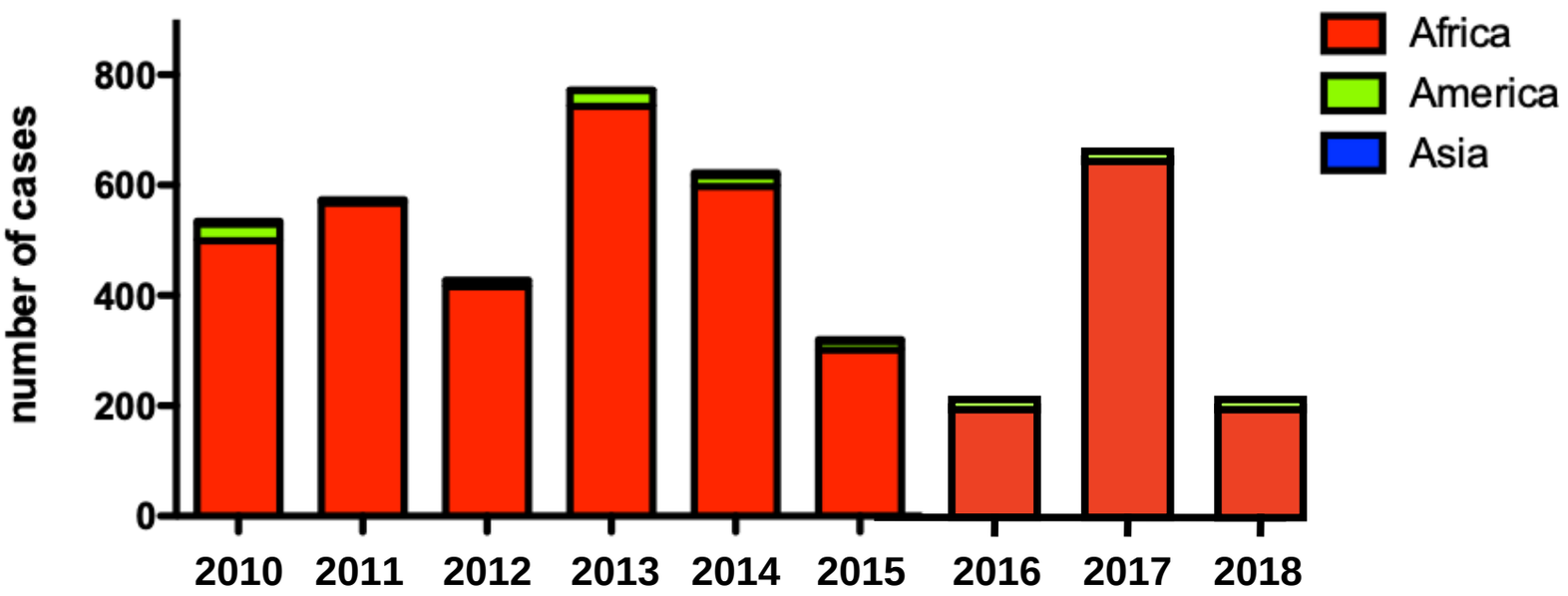
INSTITUT PASTEUR
Yersinia Research Unit

Death toll of historical pandemics



World Plague Distribution (2016)





Plague:

5 players in a complex ecosystem

Yersinia pestis

1

Agent

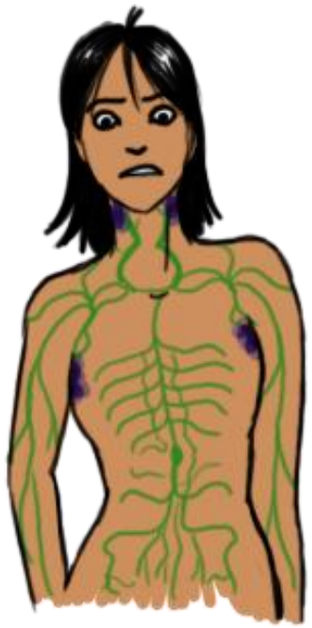
4

Environment

Fleas

3

Vector

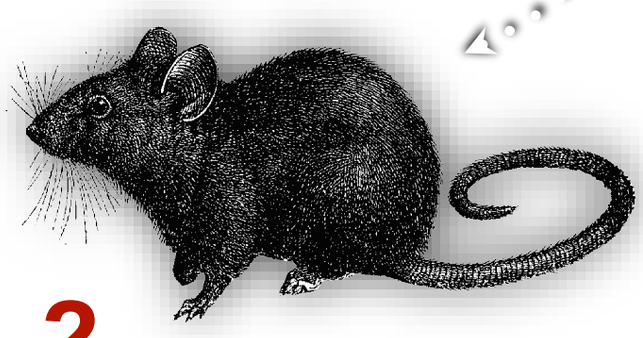


Accidental

Secondary Host

5

Rodents



2

Reservoir

>280 flea species have been reported as *Y. pestis* vectors

>270 rodent species have been detected as *Y. pestis* reservoirs

Human plague:

Three major forms: bubonic, pulmonary & septicemic

Yersinia pestis

1 **Agent**

4 **Environment**

Fleas

3 **Vector**

Rodents

2 **Reservoir**

Bubonic Plague

40-70% mortality
(incubation period: 2-6 days)

Lymph nodes

Cervical Bubo

Axilar Bubo

Accidental
Secondary Host

5

Septicemic Plague

Pneumonic Plague

Lungs

70-100% mortality
(24-72 hours)

The recent ancestor of Yersinia pestis

is the enteropathogen Y. pseudotuberculosis

Food

Letal Dose 50 (I.V.)

100 000 bacteria

Y. pseudotuberculosis

?

Flea

Letal Dose 50 (I.V.)

<10 bacteria

Yersinia pestis

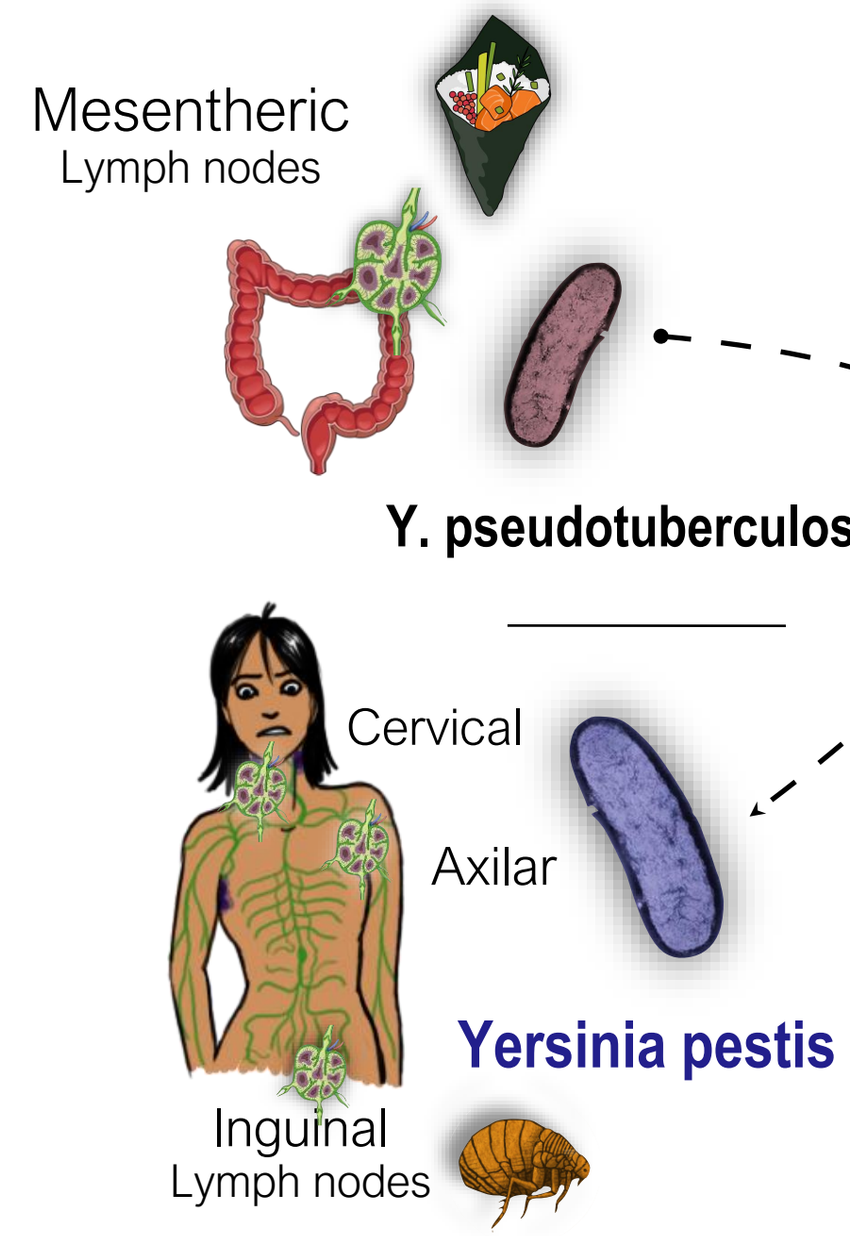
Transmission

Disease

Pathogenicity

Y. pestis shares virulence mechanisms

with the enteropathogen Y. pseudotuberculosis



Y. pestis shares virulence mechanisms

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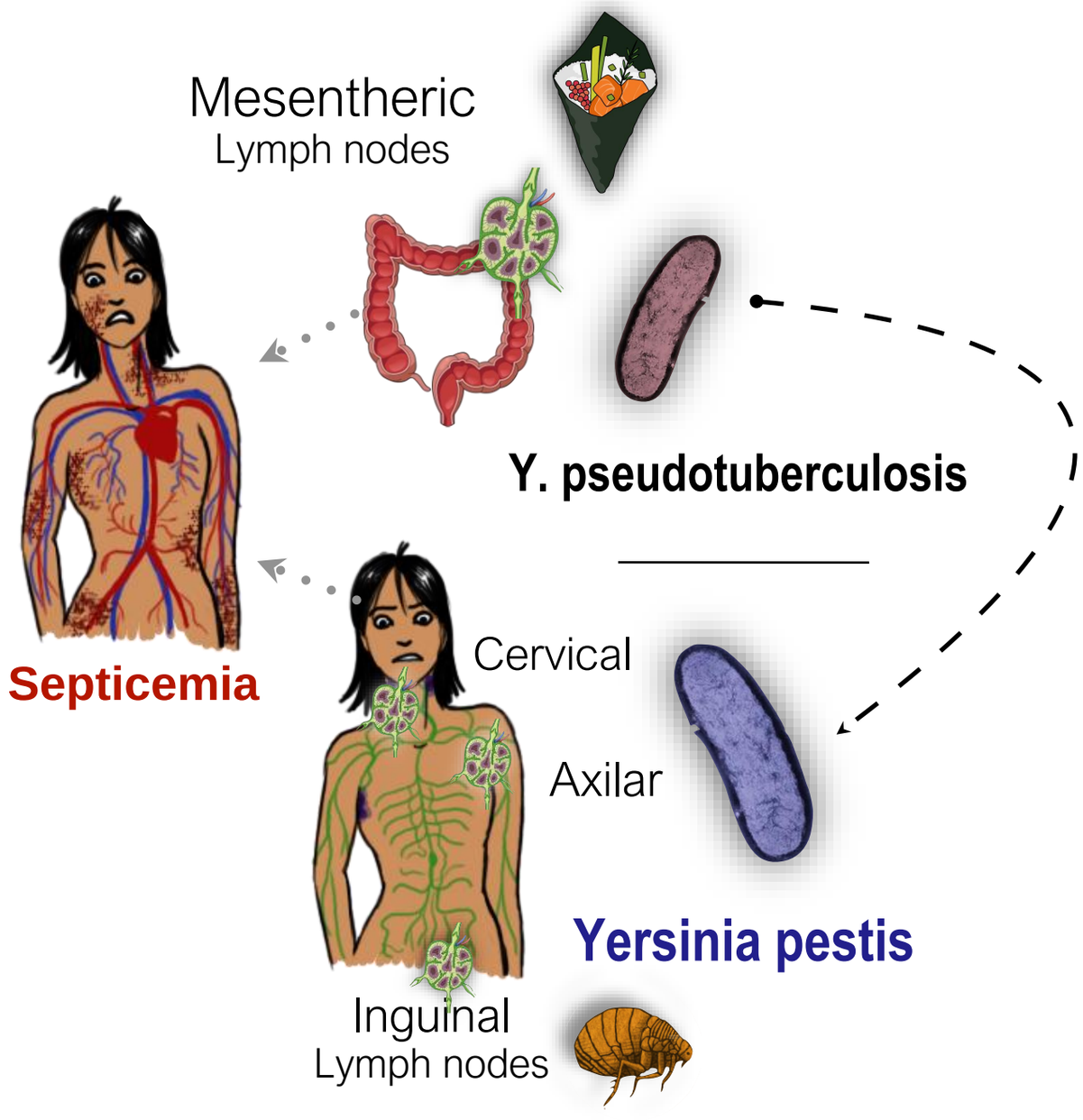
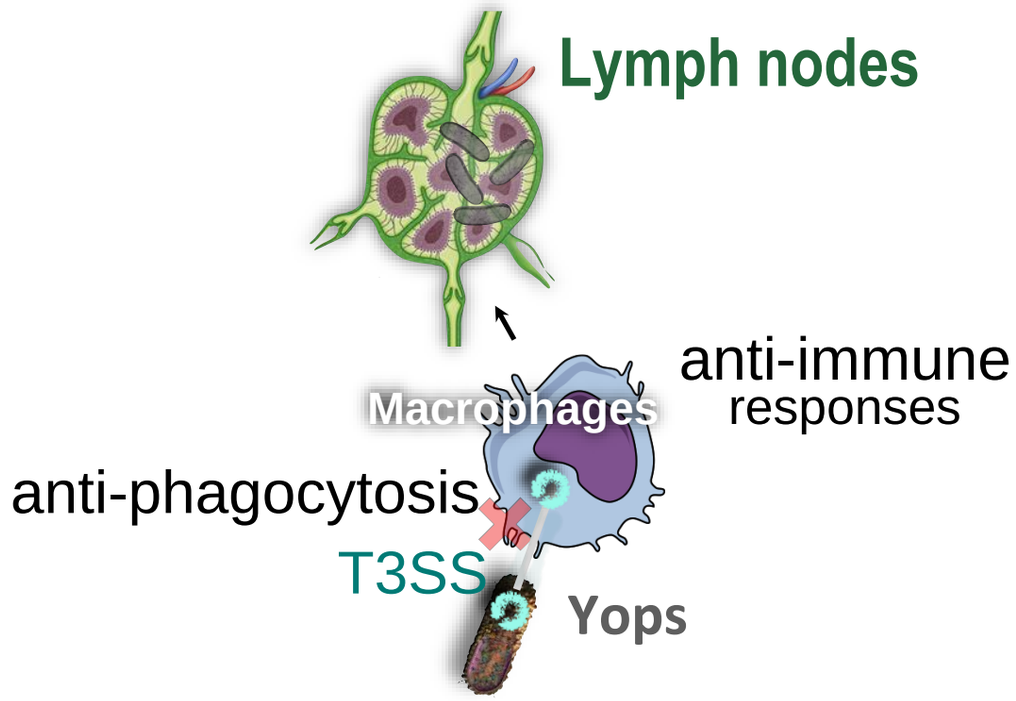
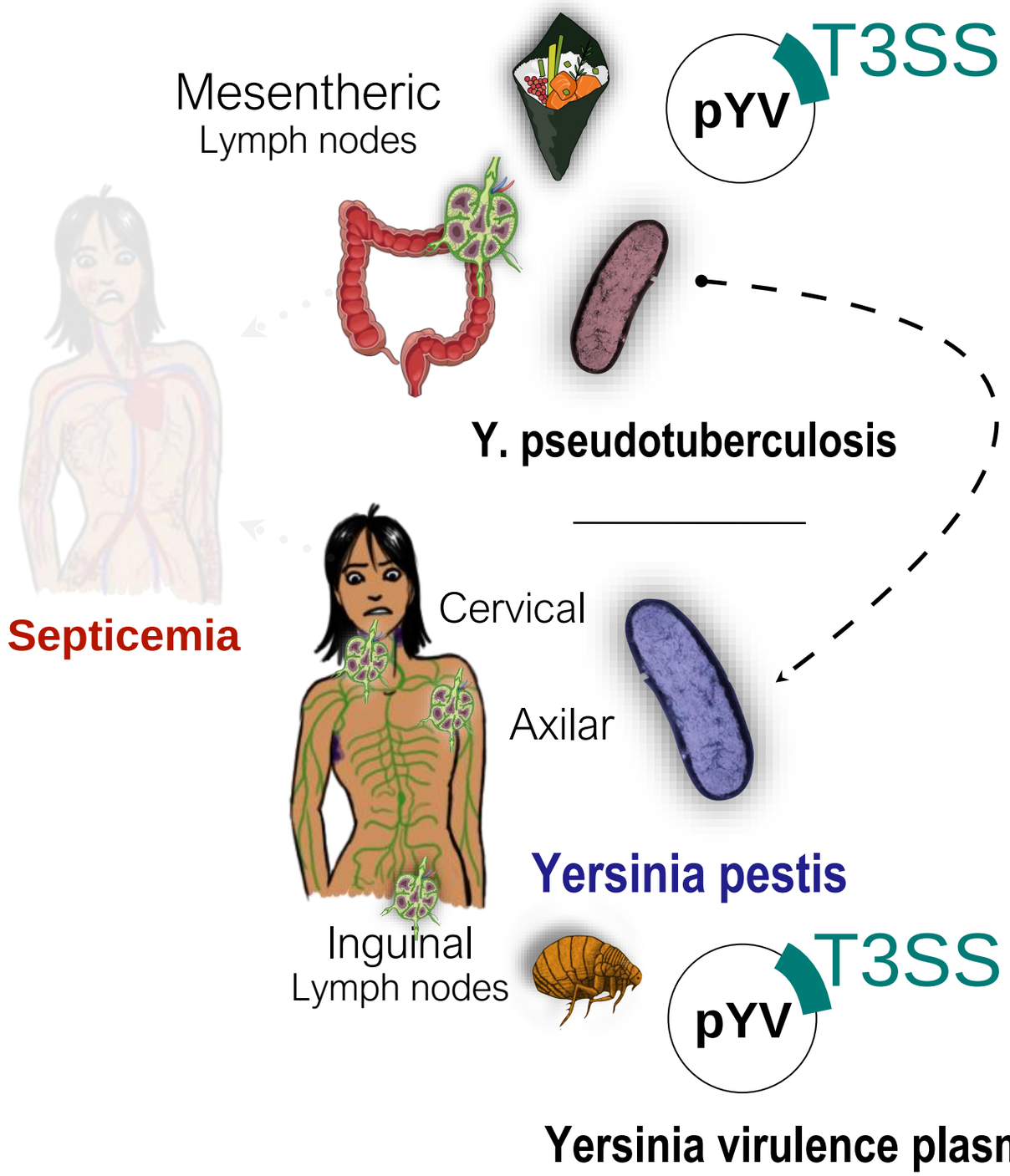


Yp & Ypstb share a Type 3 Secretion System

- a molecular syringe to inject bacterial proteins into host cells





Yp & Ypstb share an iron acquisition system

- the High Pathogenicity Island

Lymph nodes

anti-immune responses

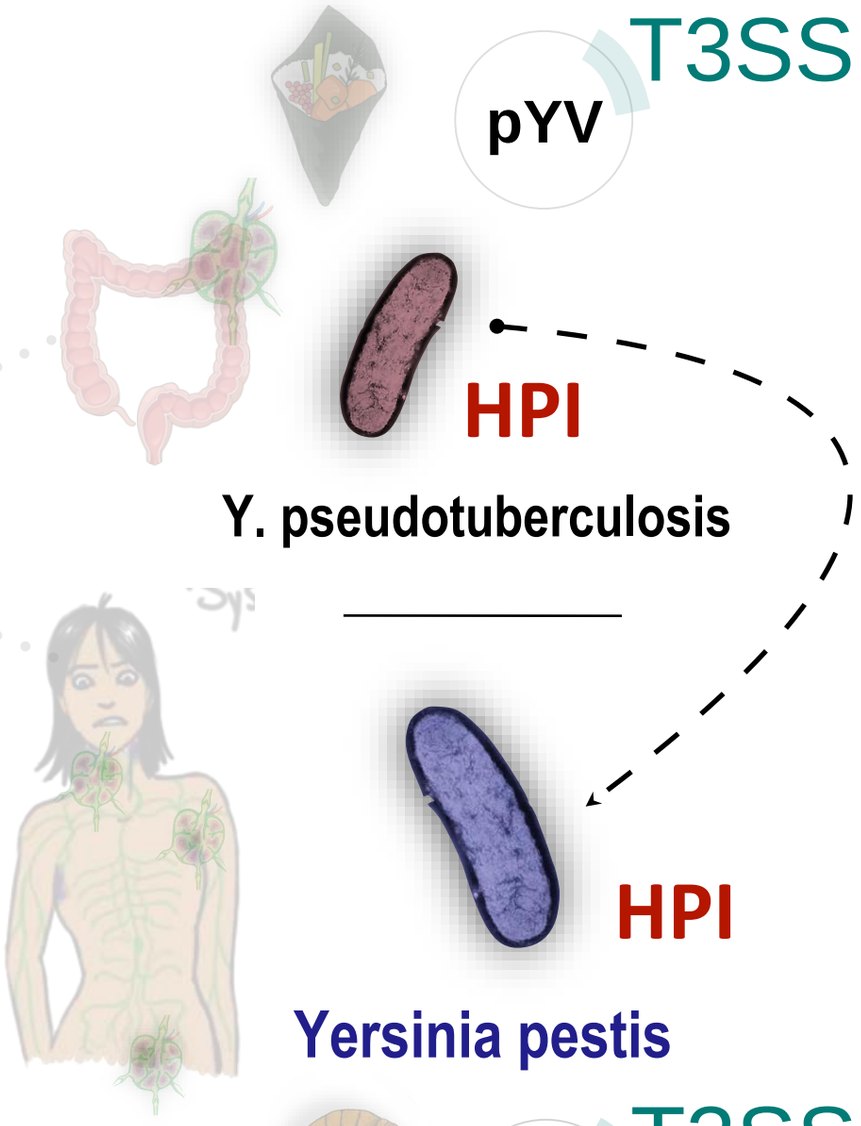
Macrophages

anti-phagocytosis

T3SS

Yops

Septicemia



T3SS

pYV

HPI

Y. pseudotuberculosis

HPI

Yersinia pestis

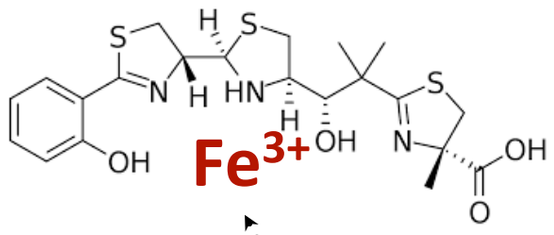
T3SS

pYV

Yersinia virulence plasmid

Yersiniabactin

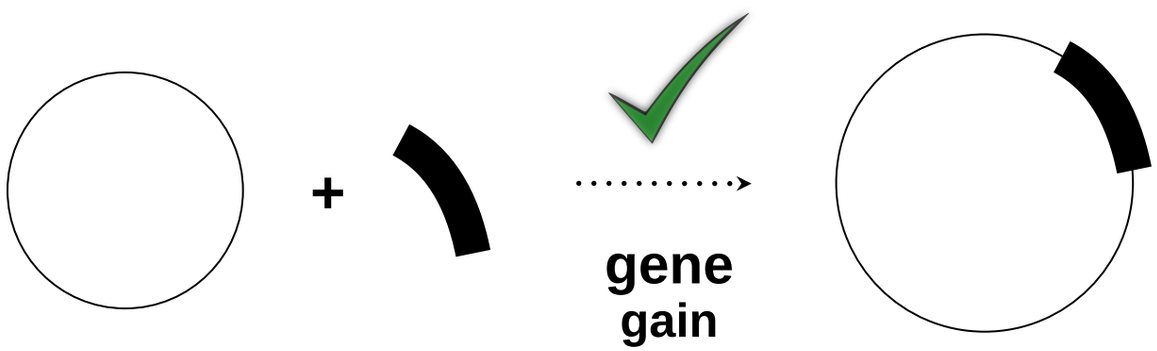
Siderophore

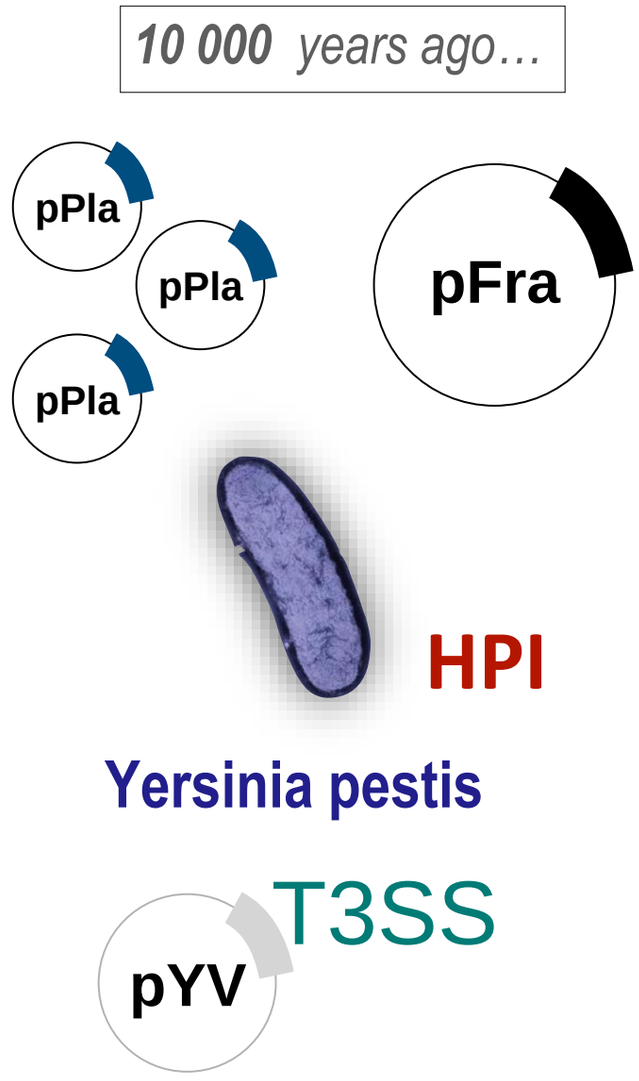


High pathogenicity island (HPI)

Yersinia pestis acquired two plasmids

critical for pathogenicity and vectoriality

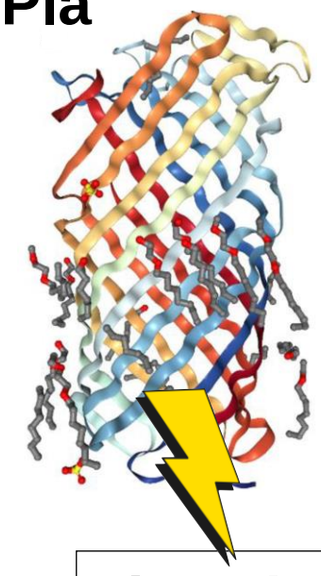




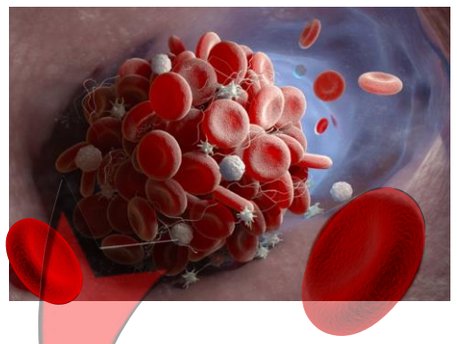
Pla is a broad-range protease

that favors **Yp** dispersion from lymph nodes & lungs

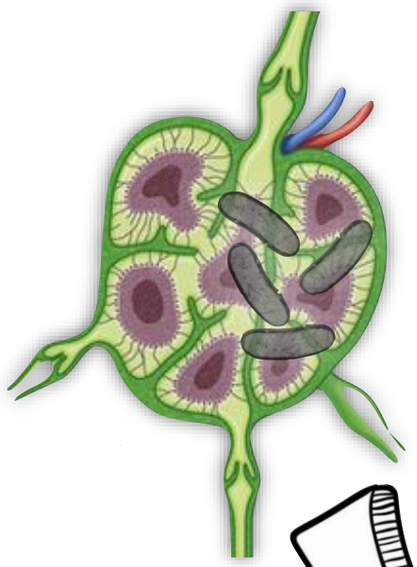
Pla

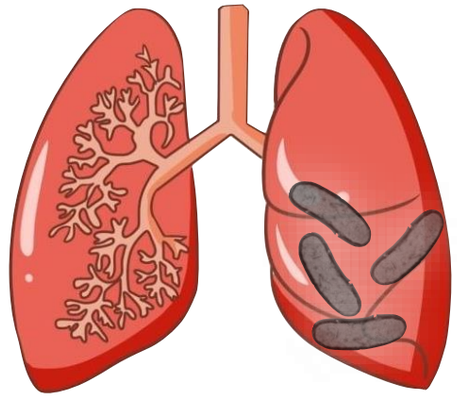


Plasminogen

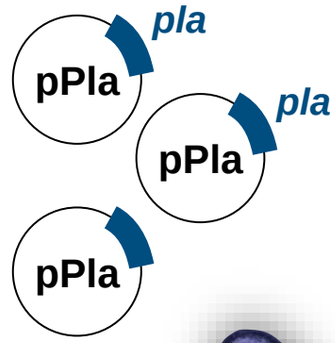


Coagulation disruption





Dispersion to other organs



pFra

HPI

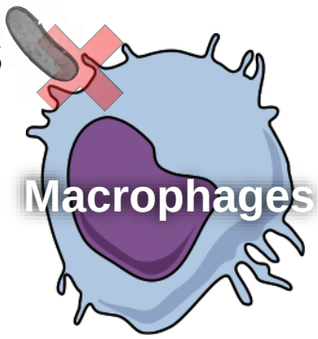
Yersinia pestis

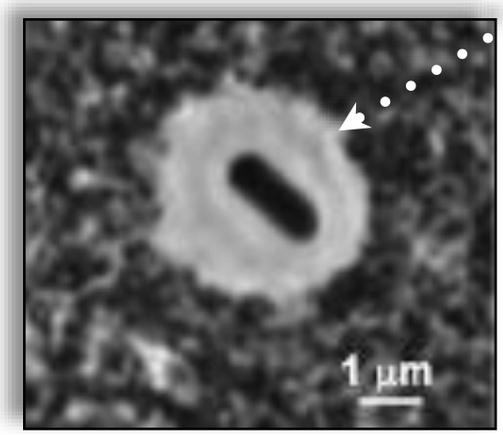
T3SS

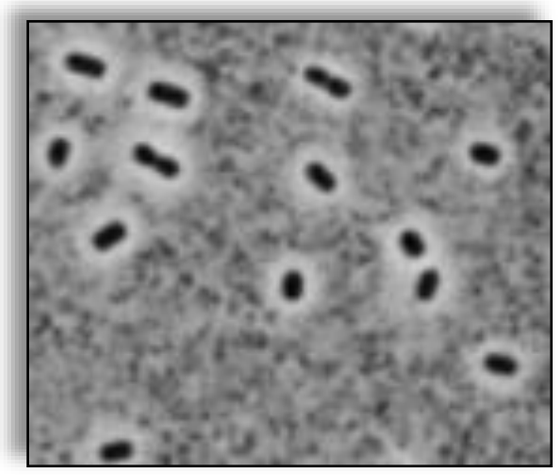
F1 forms a pseudocapsule

that hampers **Yp** phagocytosis

anti-phagocytosis







Pseudocapsule

F1

caf1

pPla

pPla

pPla

pFra

HPI

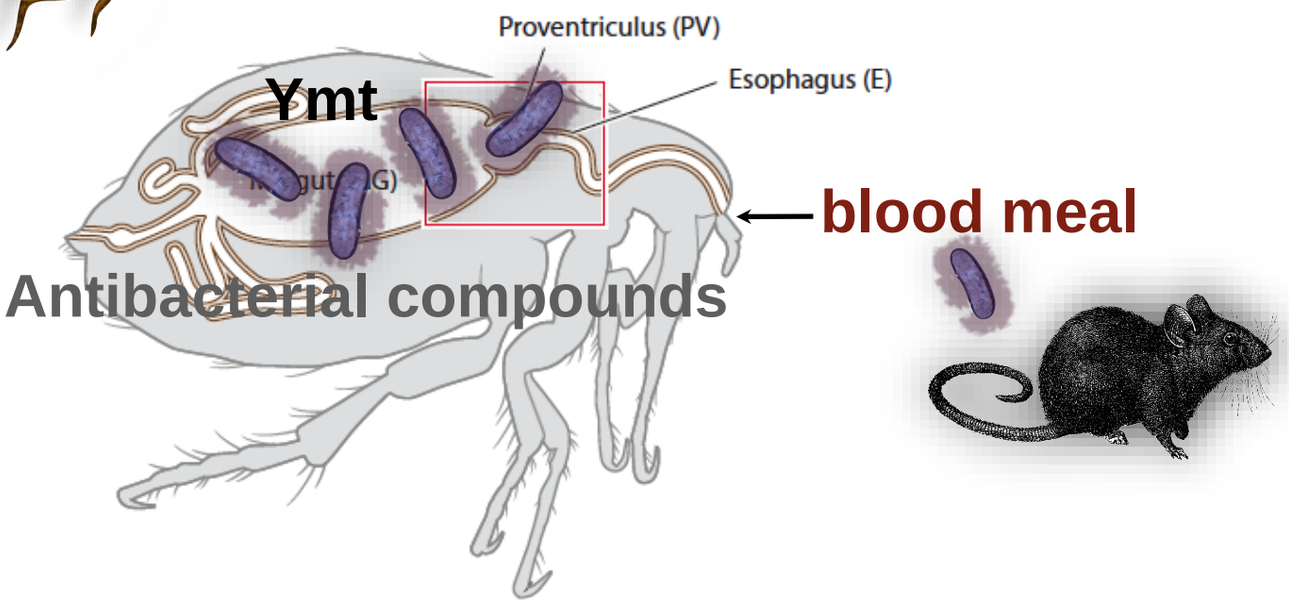
Yersinia pestis

pYV

T3SS

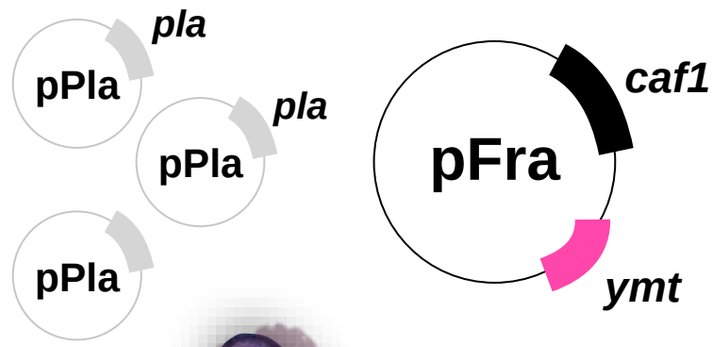
Ymt encodes a phospholipase

critical for *Y. pestis* survival in the flea intestine



blood meal

5 000 years ago…



HPI

Yersinia pestis

T3SS

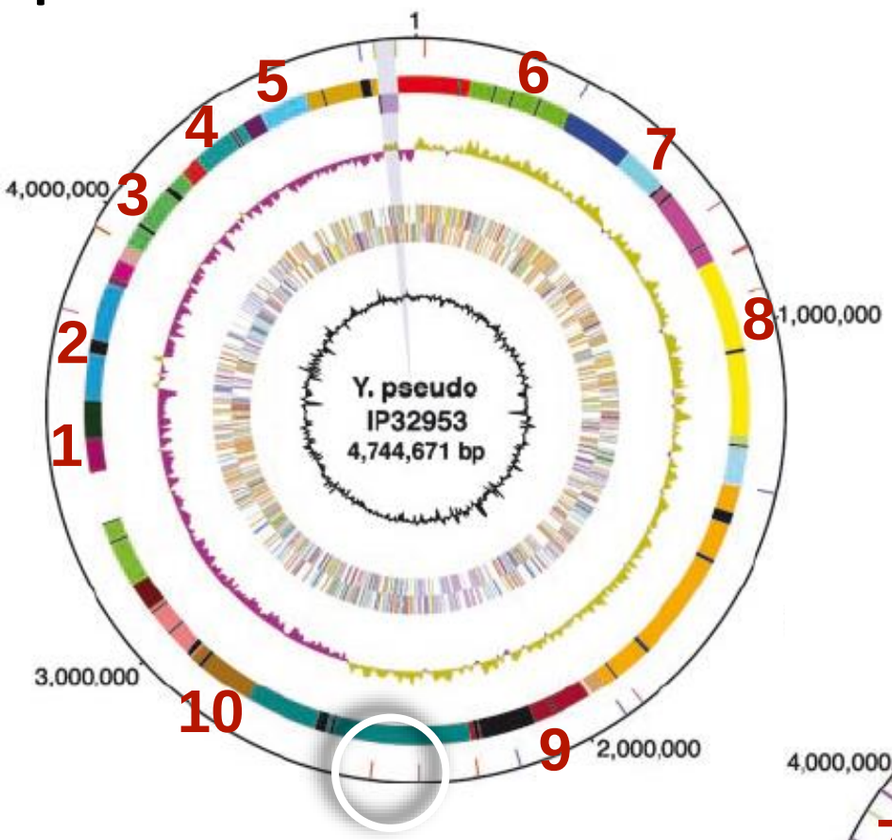
pYV

Gene inactivation

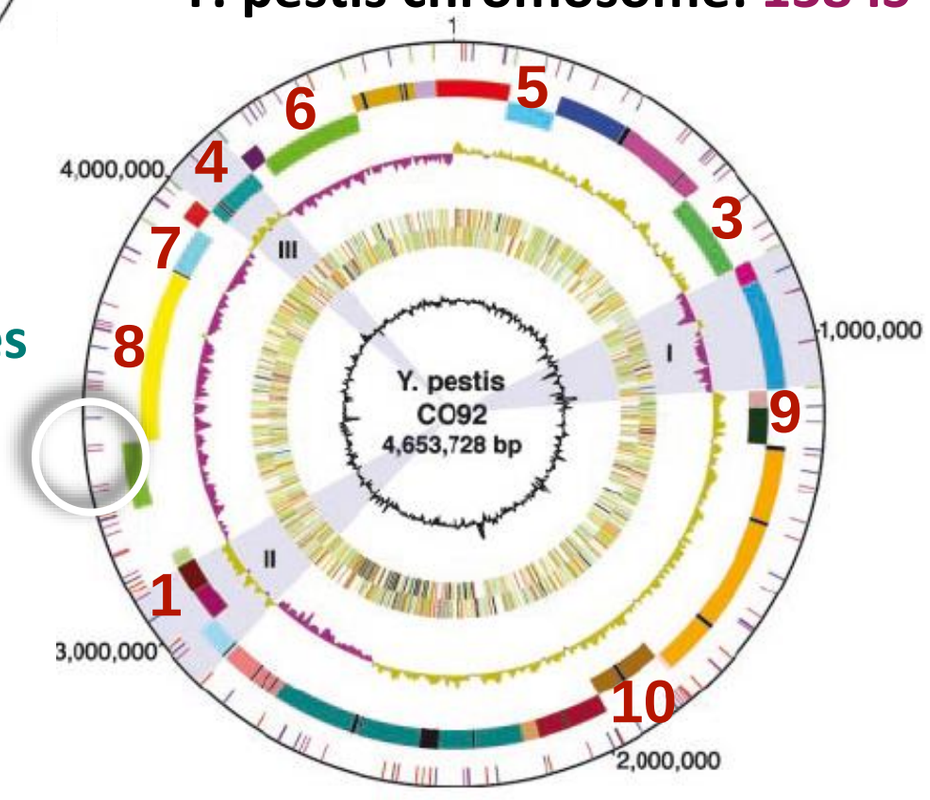
has been a major driver of *Y. pestis* evolution

1. genome rearrangements
2. insertion sequences
3. non-sense point mutations

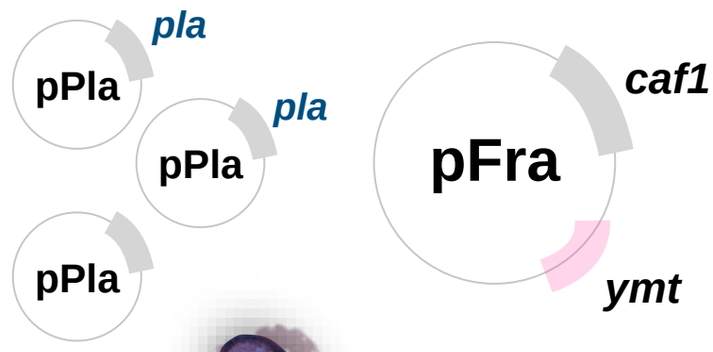
Y. pseudotuberculosis chromosome: 20 IS

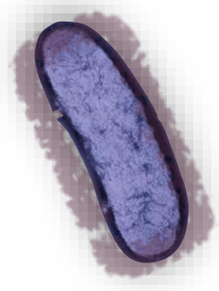


Y. pestis chromosome: 138 IS



insertion sequences





HPI

Yersinia pestis

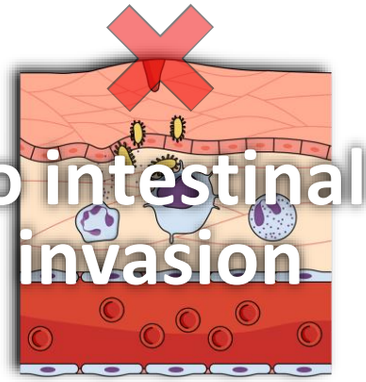
13% of the genome

is inactivated in *Y. pestis*

Gene inactivation impacted host tropism

& escape from immune responses

inv

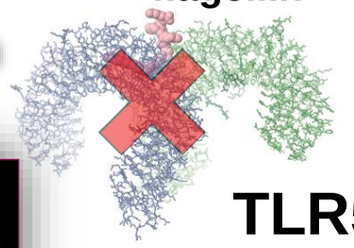


no intestinal invasion

fla

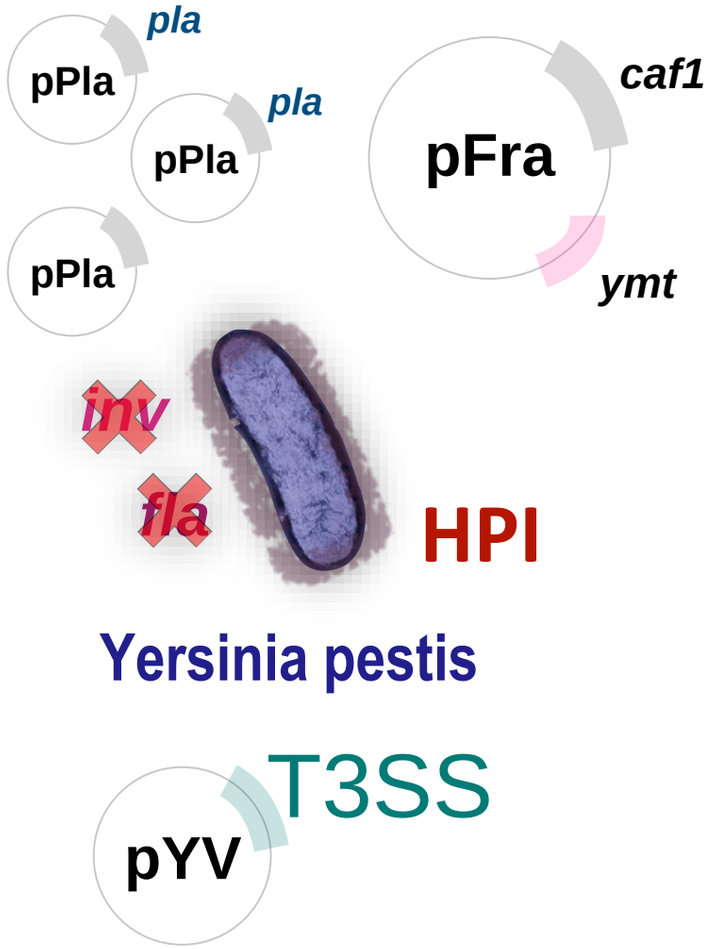
no TLR5 recognition

flagellin



TLR5

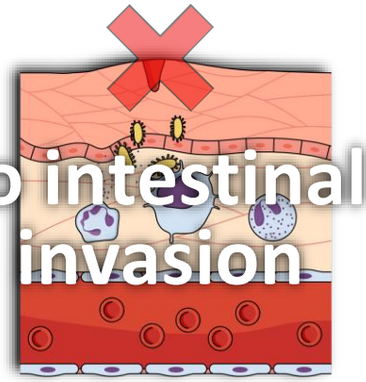
no bacterial motility



Gene inactivation impacted host tropism

& escape from immune responses

inv



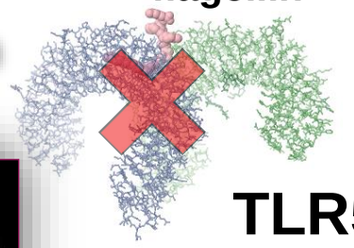
no intestinal invasion

fla

no bacterial motility

no TLR5 recognition

flagellin



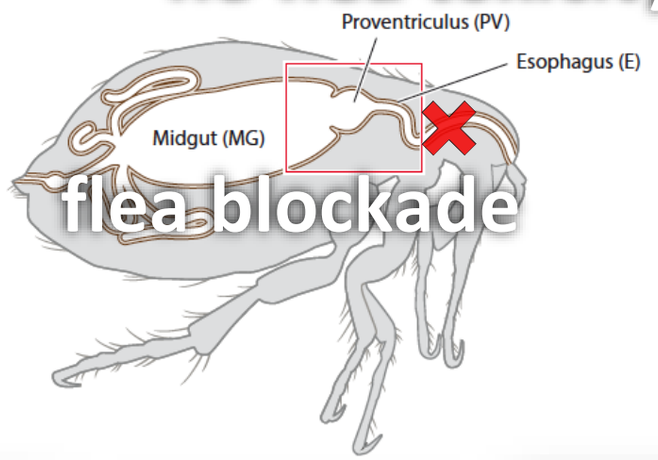
TLR5

rcs

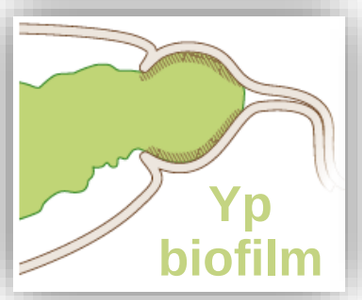
hms

no flea toxicity

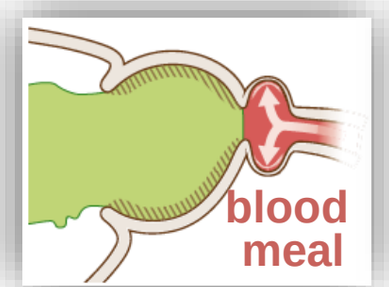
ure



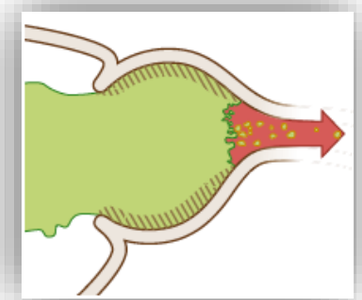
flea blockade

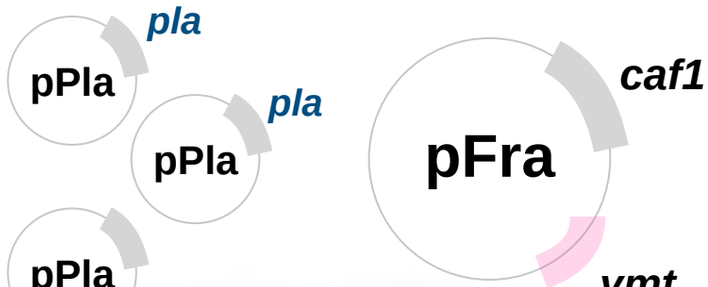


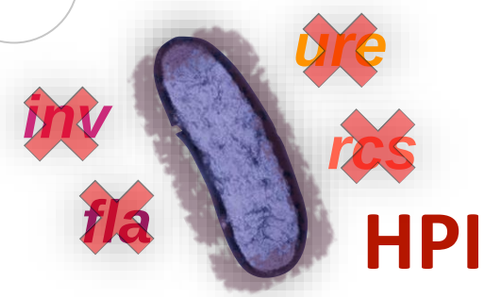
Yp biofilm



blood meal

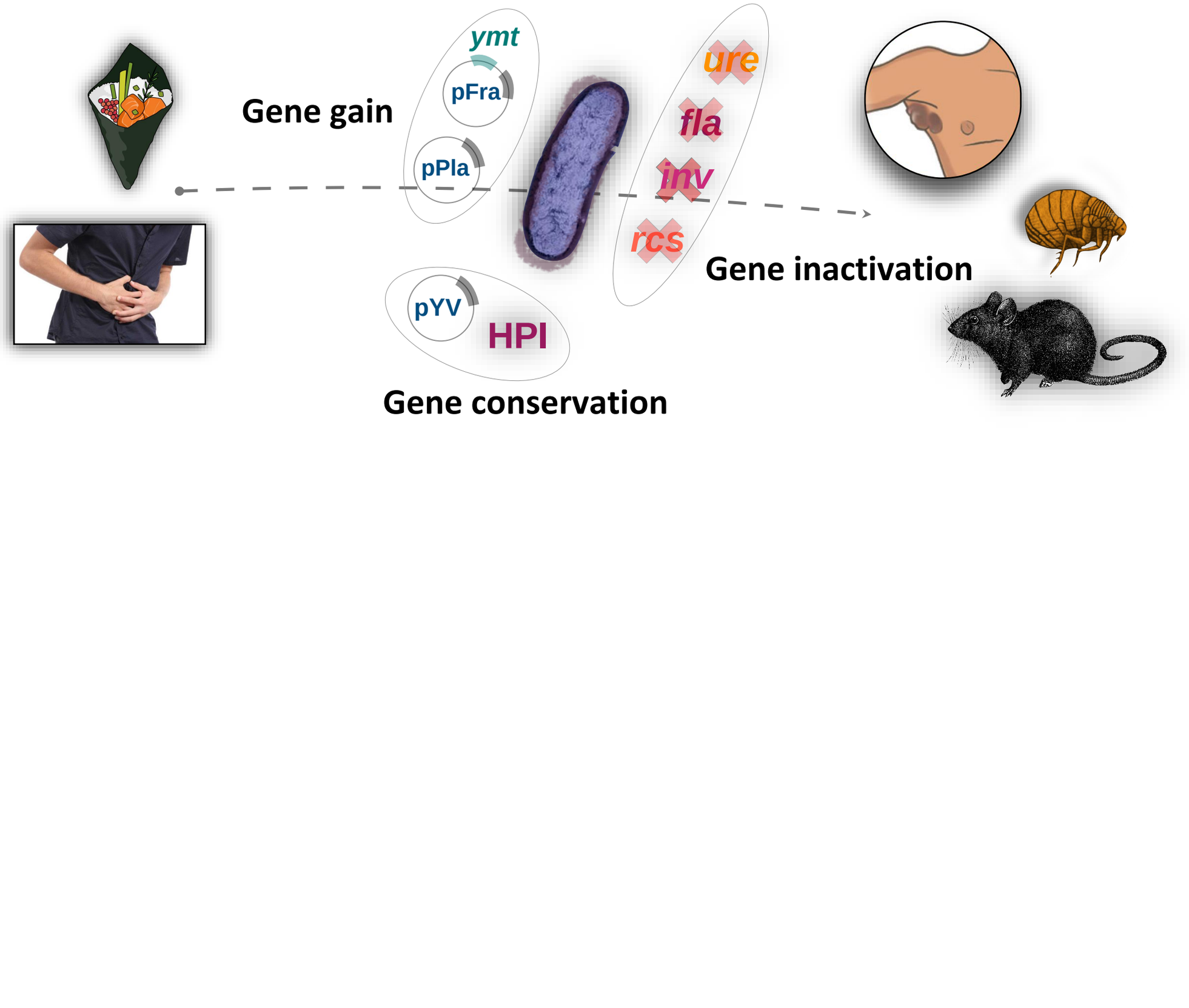






Yersinia pestis

Take Home Messages



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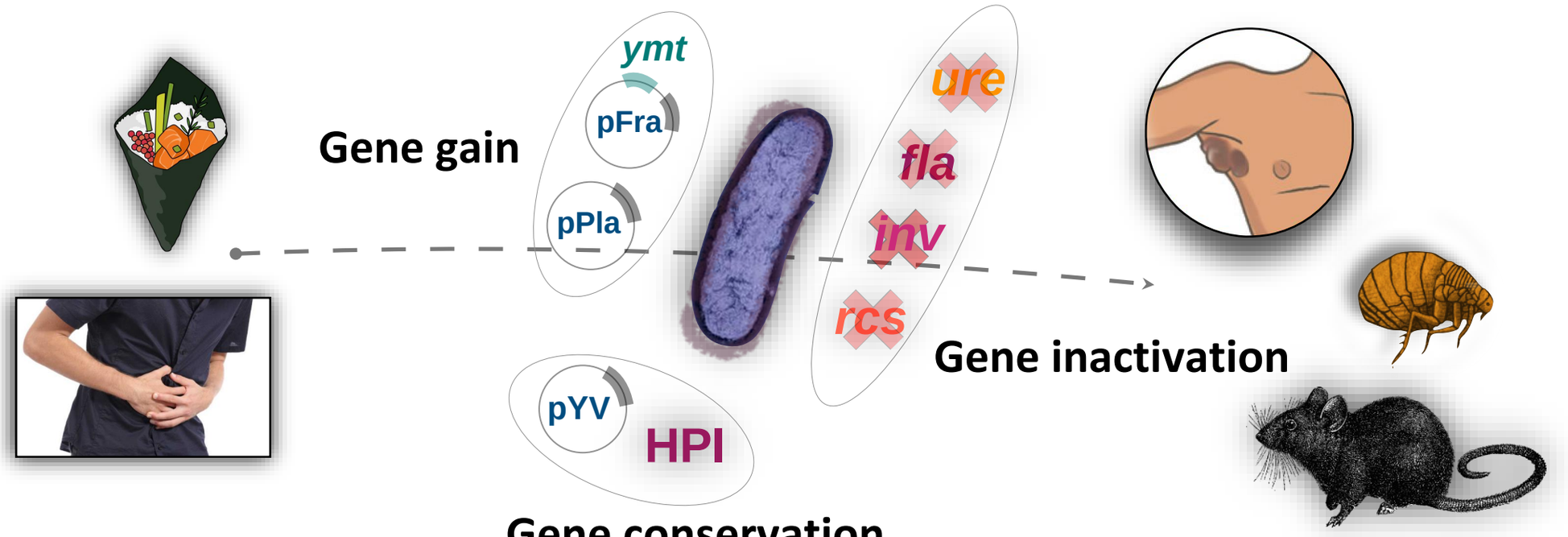

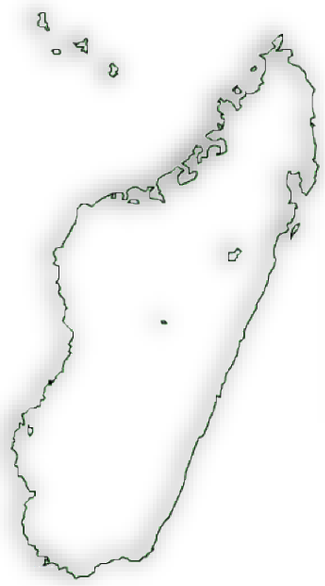

Madagascar
1997

8 MULTIDRUG RESISTANCE IN *YERSINIA PESTIS* MEDIATED BY A TRANSFERABLE PLASMID

N Engl J Med **337**: 667

Pathogen X
August 29th-30th, 2022

Bacterial evolution & Plague

Thank you!

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World Health Organization
Collaborating Centre for Plague (FRA-140)

NATIONAL REFERENCE LABORATORY
Plague & Other Yersinioses

INSTITUT PASTEUR
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