Pathogenesis of *Pseudomonas*

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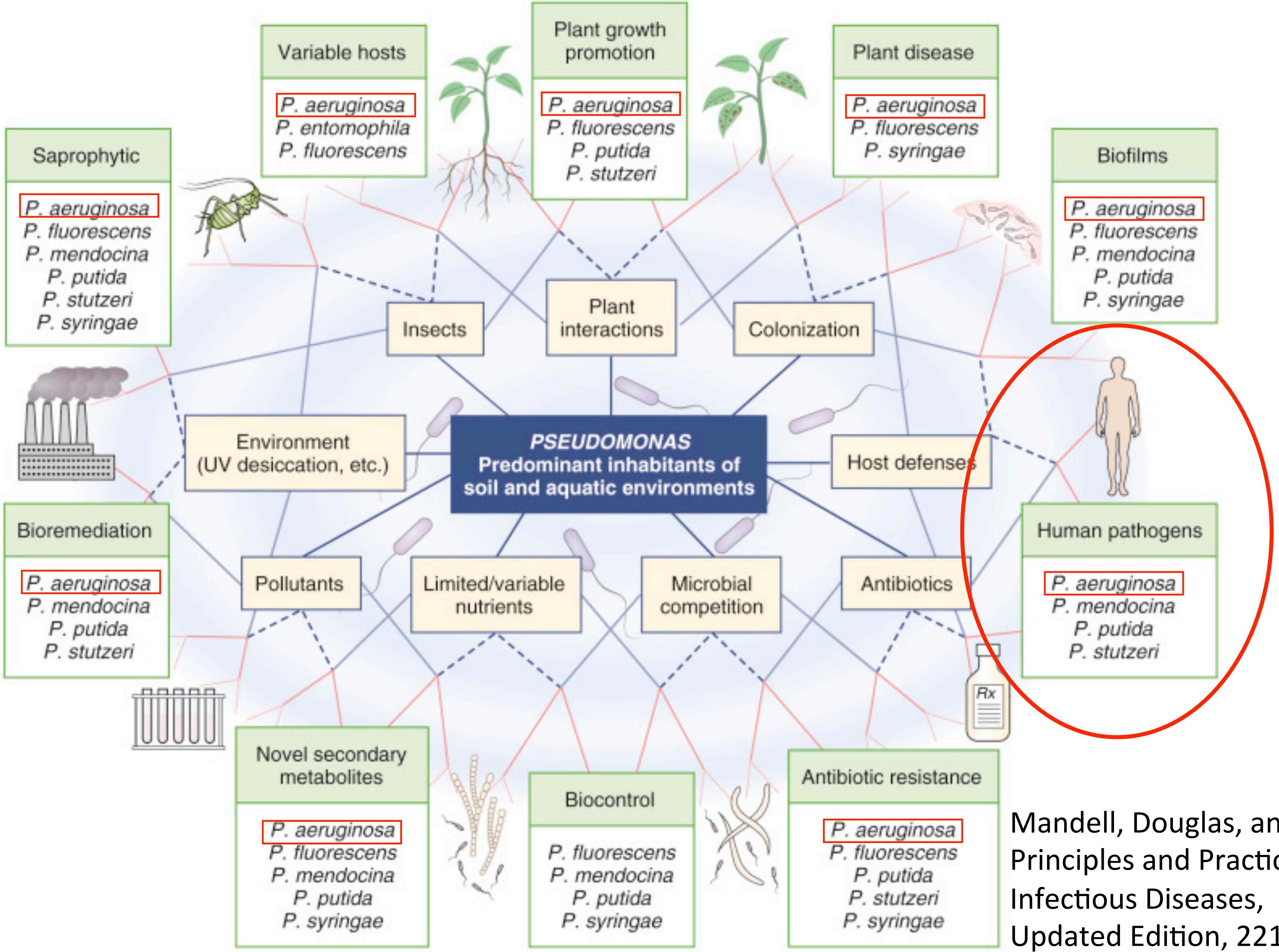
Nothing to disclose



PSEUDOMONAS
Predominant inhabitants of soil and aquatic environments

Insects

Plant interactions

Colonization

Environment (UV desiccation, etc.)

Host defenses

Pollutants

Limited/variable nutrients

Microbial competition

Antibiotics

Saprophytic
- *P. aeruginosa*
- *P. fluorescens*
- *P. mendocina*
- *P. putida*
- *P. stutzeri*
- *P. syringae*

Variable hosts
- *P. aeruginosa*
- *P. entomophila*
- *P. fluorescens*

Plant growth promotion
- *P. aeruginosa*
- *P. fluorescens*
- *P. putida*
- *P. stutzeri*

Plant disease
- *P. aeruginosa*
- *P. fluorescens*
- *P. syringae*

Biofilms
- *P. aeruginosa*
- *P. fluorescens*
- *P. mendocina*
- *P. putida*
- *P. syringae*

Bioremediation
- *P. aeruginosa*
- *P. mendocina*
- *P. putida*
- *P. stutzeri*

Human pathogens
- *P. aeruginosa*
- *P. mendocina*
- *P. putida*
- *P. stutzeri*

Novel secondary metabolites
- *P. aeruginosa*
- *P. fluorescens*
- *P. mendocina*
- *P. putida*
- *P. syringae*

Biocontrol
- *P. fluorescens*
- *P. mendocina*
- *P. putida*
- *P. syringae*

Antibiotic resistance
- *P. aeruginosa*
- *P. fluorescens*
- *P. putida*
- *P. stutzeri*
- *P. syringae*

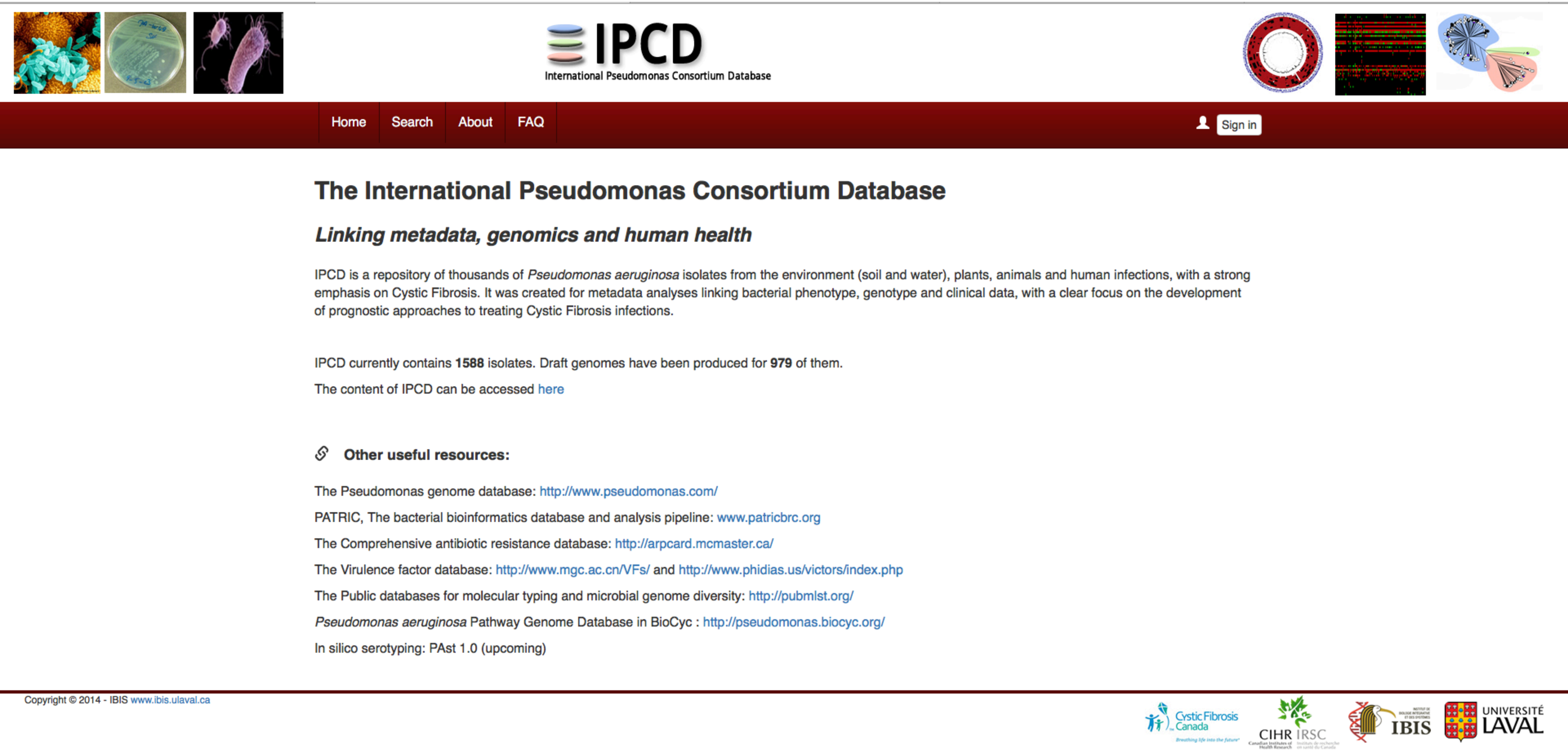
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Updated Edition, 221, 2518-2531.e3

P. aeruginosa physiology

- Ubiquitous
- Minimal growth requirements
- Temperature
- Can grow anaerobically with arginine or nitrate
- Resistant to antimicrobials
  - Permeability barrier
  - Numerous efflux pumps
  - Acquired resistance

What is available to the field?

- Strains
  - First sequenced *P. aeruginosa* strain, PAO1 (Stover et al. Nature 2000)
    - Large genome, single circular chromosome, ~6.6 Mb
    - >5580 ORF
    - 66% G+C
- Bioinformatic analysis
- Ordered transposon (Tn) libraries
  - PAO1, Jacobs et al. PNAS 2003
  - PA14, Liberati et al. PNAS 2006
- State of the art genetic tools
  - Reagents for the construction of specific mutations
  - Tnseq
  - RNAseq



The International Pseudomonas Consortium Database

Linking metadata, genomics and human health

IPCD is a repository of thousands of *Pseudomonas aeruginosa* isolates from the environment (soil and water), plants, animals and human infections, with a strong emphasis on Cystic Fibrosis. It was created for metadata analyses linking bacterial phenotype, genotype and clinical data, with a clear focus on the development of prognostic approaches to treating Cystic Fibrosis infections.

IPCD currently contains **1588** isolates. Draft genomes have been produced for **979** of them.

The content of IPCD can be accessed here

Other useful resources:

The Pseudomonas genome database: http://www.pseudomonas.com/

PATRIC, The bacterial bioinformatics database and analysis pipeline: www.patricbrc.org

The Comprehensive antibiotic resistance database: http://arpcard.mcmaster.ca/

The Virulence factor database: http://www.mgc.ac.cn/VFs/ and http://www.phidias.us/victors/index.php

The Public databases for molecular typing and microbial genome diversity: http://pubmlst.org/

Pseudomonas aeruginosa Pathway Genome Database in BioCyc : http://pseudomonas.biocyc.org/

In silico serotyping: PAst 1.0 (upcoming)

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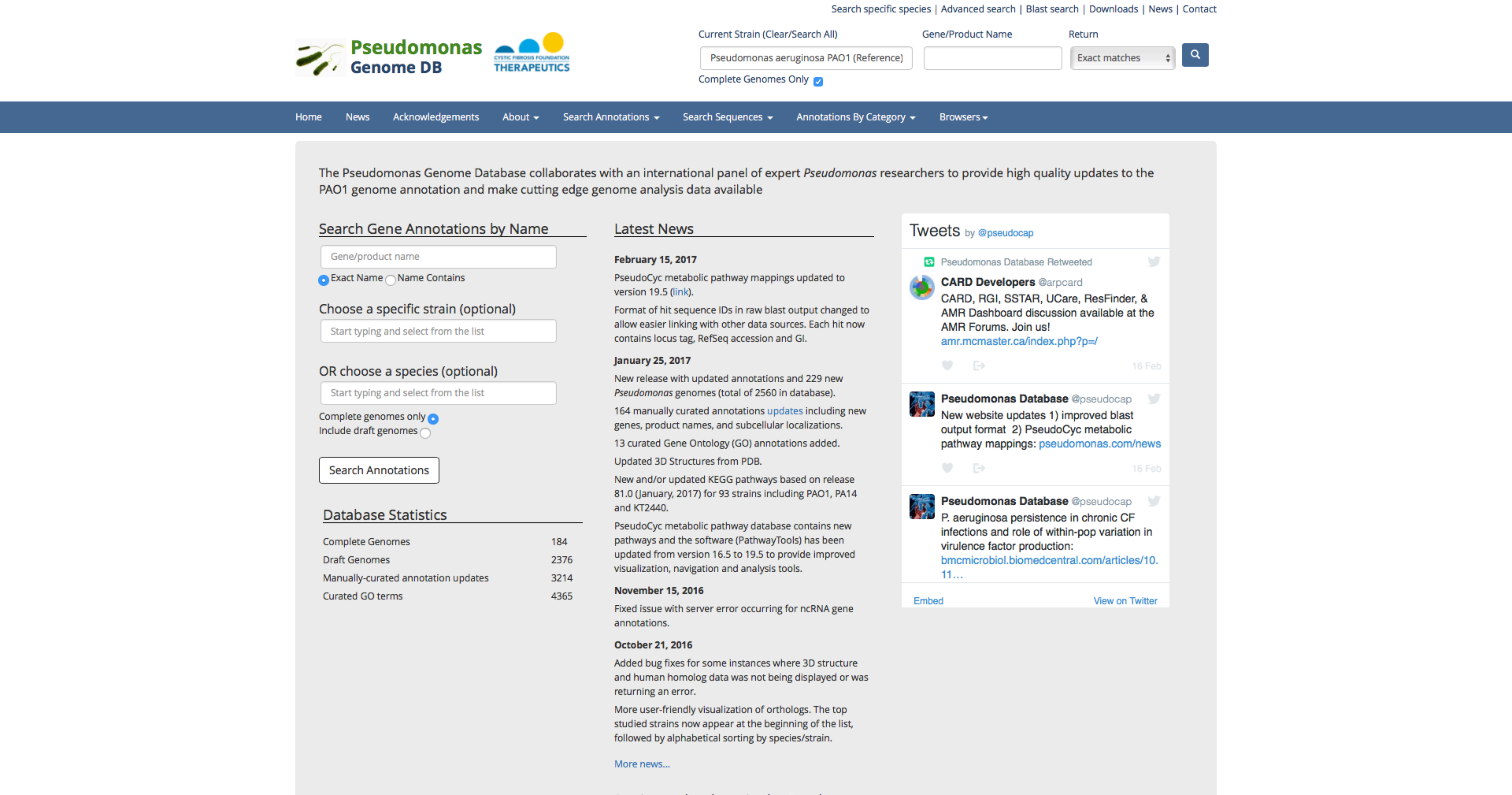

Current Strain (Clear/Search All): Pseudomonas aeruginosa PAO1 (Reference)

Gene/Product Name

Return: Exact matches

Complete Genomes Only ☑

The Pseudomonas Genome Database collaborates with an international panel of expert *Pseudomonas* researchers to provide high quality updates to the PAO1 genome annotation and make cutting edge genome analysis data available

Search Gene Annotations by Name

Gene/product name

● Exact Name ○ Name Contains

Choose a specific strain (optional)

Start typing and select from the list

OR choose a species (optional)

Start typing and select from the list

Complete genomes only ●
Include draft genomes ○

Database Statistics

Complete Genomes	184
Draft Genomes	2376
Manually-curated annotation updates	3214
Curated GO terms	4365

Latest News

February 15, 2017

PseudoCyc metabolic pathway mappings updated to version 19.5 (link).

Format of hit sequence IDs in raw blast output changed to allow easier linking with other data sources. Each hit now contains locus tag, RefSeq accession and GI.

January 25, 2017

New release with updated annotations and 229 new *Pseudomonas* genomes (total of 2560 in database).

164 manually curated annotations updates including new genes, product names, and subcellular localizations.

13 curated Gene Ontology (GO) annotations added.

Updated 3D Structures from PDB.

New and/or updated KEGG pathways based on release 81.0 (January, 2017) for 93 strains including PAO1, PA14 and KT2440.

PseudoCyc metabolic pathway database contains new pathways and the software (PathwayTools) has been updated from version 16.5 to 19.5 to provide improved visualization, navigation and analysis tools.

November 15, 2016

Fixed issue with server error occurring for ncRNA gene annotations.

October 21, 2016

Added bug fixes for some instances where 3D structure and human homolog data was not being displayed or was returning an error.

More user-friendly visualization of orthologs. The top studied strains now appear at the beginning of the list, followed by alphabetical sorting by species/strain.

More news...

Tweets by @pseudocap

Pseudomonas Database Retweeted

CARD Developers @arpcard

CARD, RGI, SSTAR, UCare, ResFinder, & AMR Dashboard discussion available at the AMR Forums. Join us! amr.mcmaster.ca/index.php?p=/

16 Feb

Pseudomonas Database @pseudocap

New website updates 1) improved blast output format 2) PseudoCyc metabolic pathway mappings: pseudomonas.com/news

16 Feb

Pseudomonas Database @pseudocap

P. aeruginosa persistence in chronic CF infections and role of within-pop variation in virulence factor production: bmcmicrobiol.biomedcentral.com/articles/10.11…

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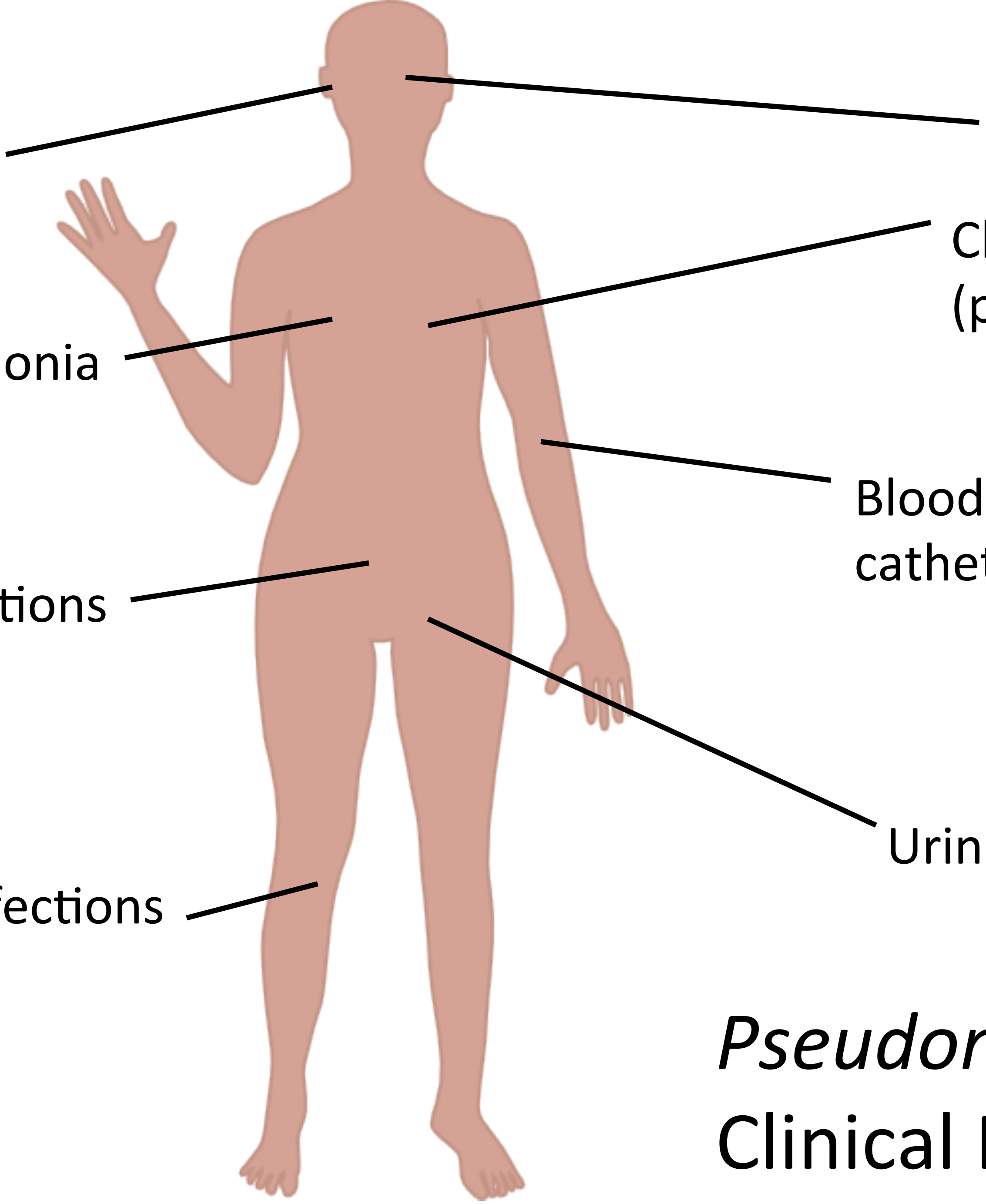
P. aeruginosa is an opportunistic pathogen

- Infections generally occur in the context of breach of the innate immune system
- Healthy animals like healthy humans are typically resistant to infection

Pseudomonas aeruginosa Clinical Presentation



Ear infections

Eye infections

Chronic respiratory infections (particularly, cystic fibrosis)

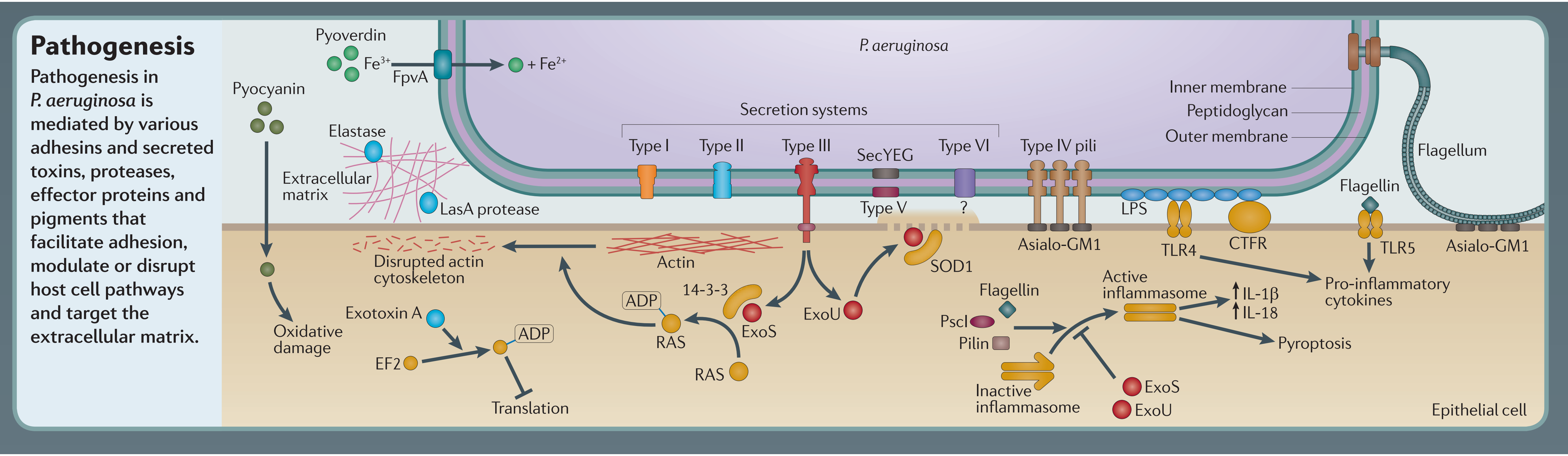
Hospital-acquired pneumonia

Bloodstream and catheter-related infections

Intra-abdominal infections

Urinary tract infections

Skin and soft tissue infections



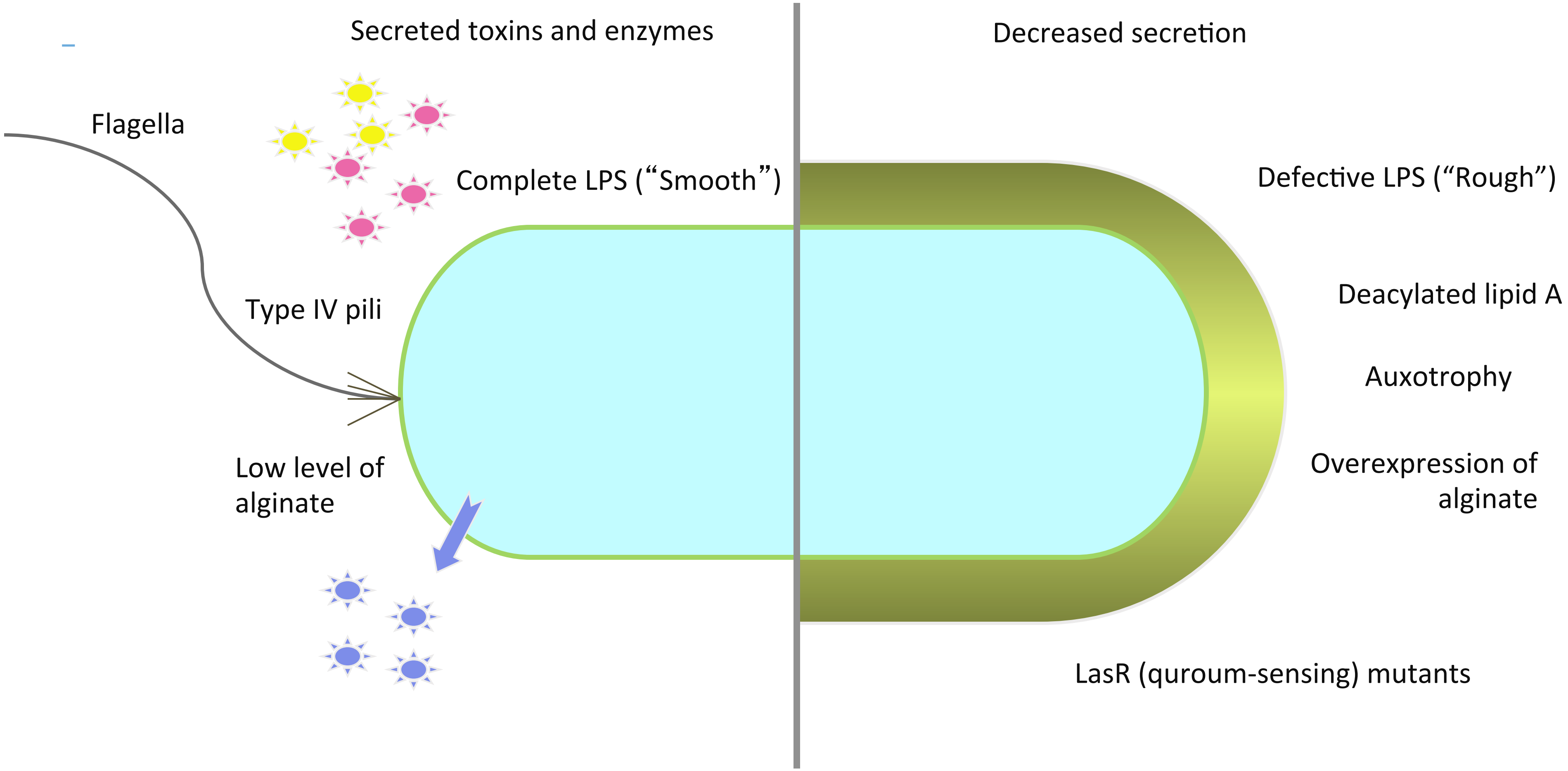
Pathogenesis

Pathogenesis in *P. aeruginosa* is mediated by various adhesins and secreted toxins, proteases, effector proteins and pigments that facilitate adhesion, modulate or disrupt host cell pathways and target the extracellular matrix.

Pseudomonas aeruginosa
Alan Hauser and Egon A. Ozer
Nature Review Microbiology
Vol. 9 no. 3 March 2011

Early (Acute) Infection

Chronic Infection



Secreted toxins and enzymes

Flagella

Complete LPS (“Smooth”)

Type IV pili

Low level of
alginate

Decreased secretion

Defective LPS (“Rough”)

Deacylated lipid A

Auxotrophy

Overexpression of
alginate

LasR (quroum-sensing) mutants

Adaptation During Chronic Lung Infection In Cystic Fibrosis

Considerations for development of animal models of *P. aeruginosa*

- Normal healthy animals are generally resistant to infection
  - Some acute infections can disseminate
  - Other infections stay localized
- *P. aeruginosa* adapts during chronic respiratory infections in cystic fibrosis (CF)
  - There are >1700 recognized disease-associated mutations in *CFTR* in the human population (with F508del being most common), but not all are equivalent
- Strains from particular sources may express distinct constellations of pathogenic factors that may be essential at different infection sites

Thanks