Why care about infection in CF?

Culture Data for Individuals Seen in 2017

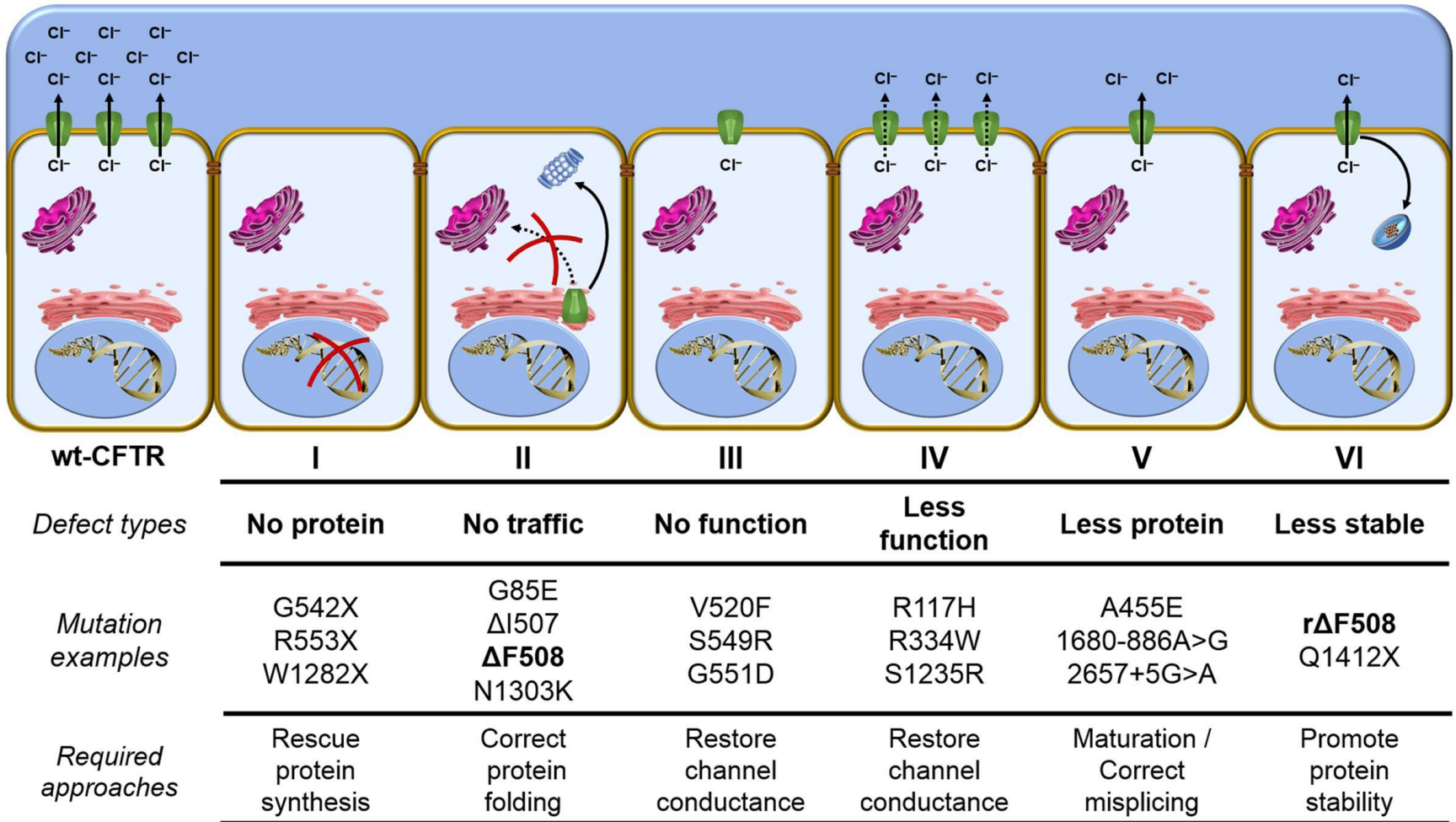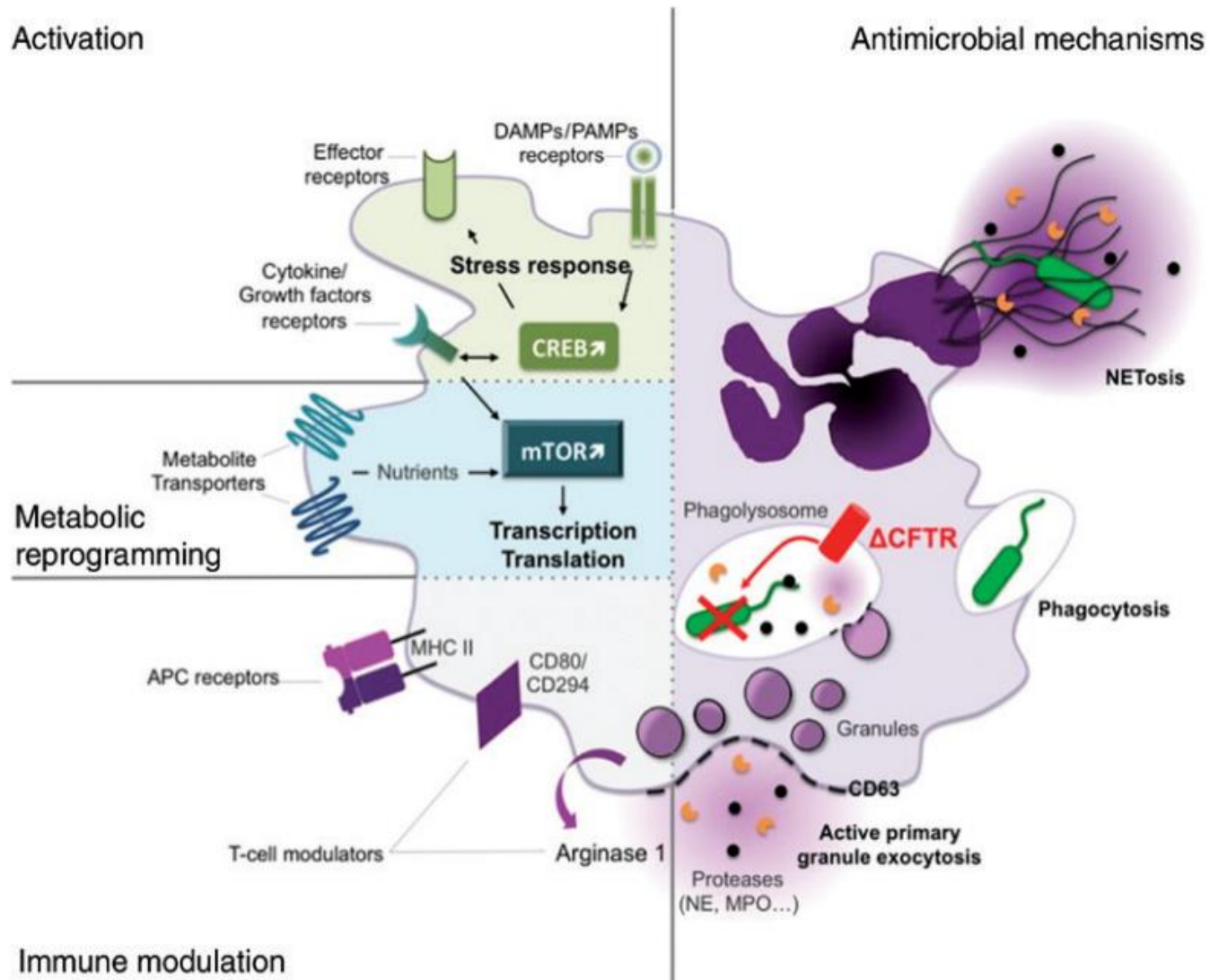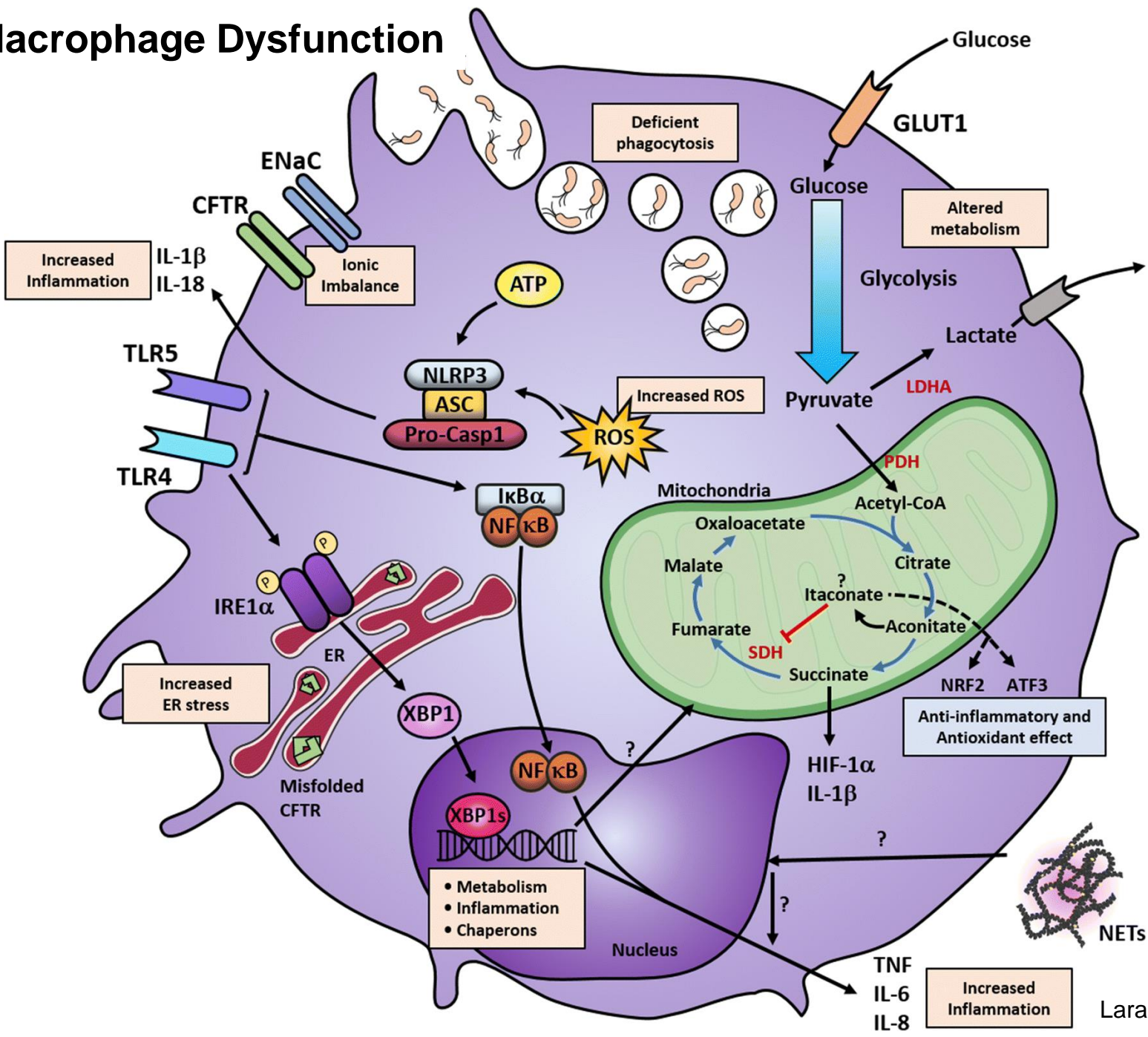|	Bacteria	Percent with Infection	Median Age in Years at First Infection	Distinctive Features in CF
⭐	P. aeruginosa	44.6	5.2	• A leading cause of airway infection • Associated with a decline in lung function • 17.9% of strains are multidrug-resistant
⭐	B. cepacia complex	2.4	19.4	• Small proportion of people with CF infected • Can lead to rapid deterioration • Multidrug-resistant
⭐	MRSA	25.2	11.1	• Prevalent among people with and without CF • Multidrug-resistant • Health care and community-associated strains
	S. maltophilia	12.6	9.4	• Found in water, soil, plants, animals, and hospital environments • Often multidrug-resistant
	Achromobacter xylosoxidans	5.8	13.8	• Inhabits natural environment, including soil and water • Often multidrug-resistant
⭐	Non-tuberculous mycobacteria	12.6	20.7	• Found in water and soil • Sporadic reports of person-to-person spread • Treatment is rigorous and often poorly tolerated

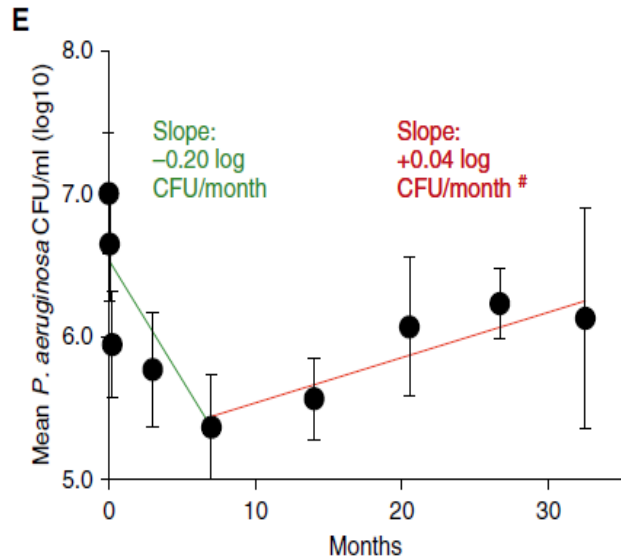www.cff.org

Mutation classes and Trikafta Mechanism

Defect types	I	II	III	IV	V	VI
	No protein	No traffic	No function	Less function	Less protein	Less stable
Mutation examples	G542X R553X W1282X	G85E ΔI507 **ΔF508** N1303K	V520F S549R G551D	R117H R334W S1235R	A455E 1680-886A>G 2657+5G>A	**rΔF508** Q1412X
Required approaches	Rescue protein synthesis	Correct protein folding	Restore channel conductance	Restore channel conductance	Maturation / Correct misplicing	Promote protein stability

wt-CFTR

Neutrophil dysfunction in CF

CF Macrophage Dysfunction

Lara-Reyna, 2020
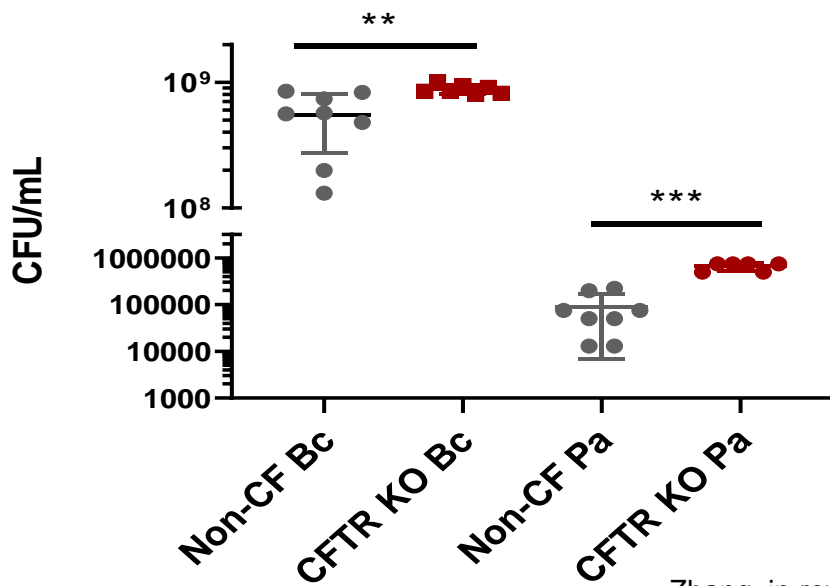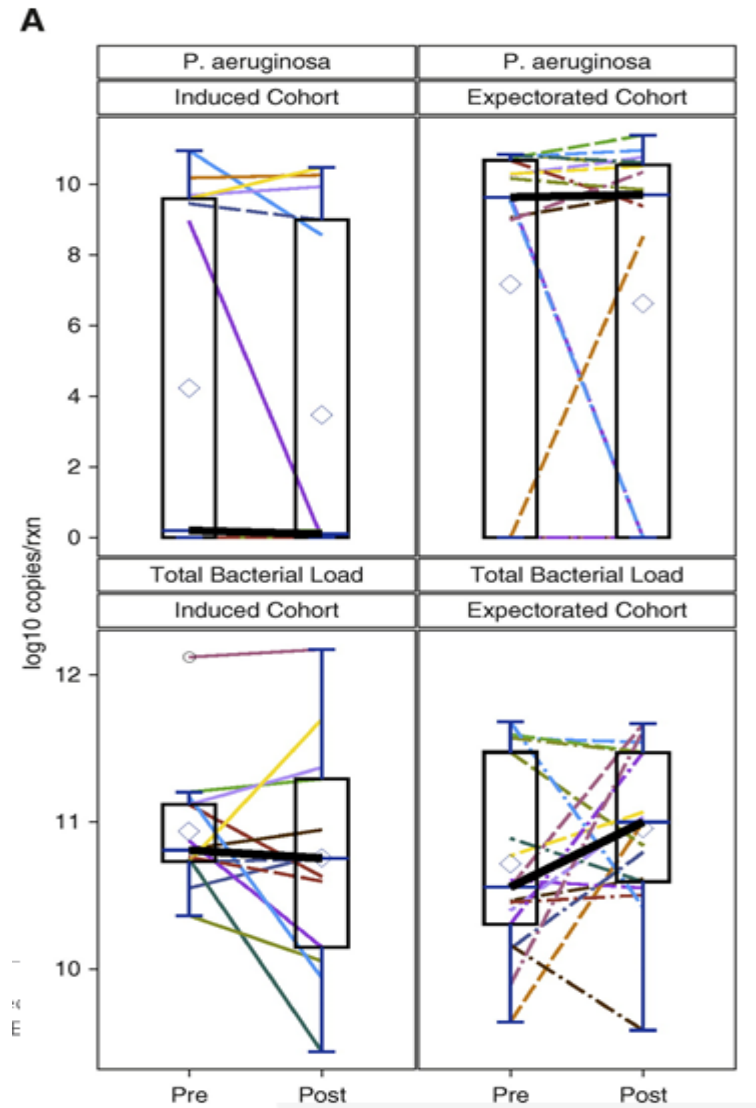
Infections persist despite CFTR modulators

Hisert, AJRCCM 2017

Zhang, in review

Harris, 2020.   Ivacaftor cohort

Opportunistic pathogens & CF immune cells

B. cenocepacia

- Reduces MΦ ROS production
- Decreases MΦ autophagy

P. aeruginosa

- Biofilms
- Exacerbated immune responses

S. aureus

- Persist intracellularly
- Autophagy subversion

NTM

- *M. abscessus*, a virulent highly antibiotic-resistant NTM
- Two colony morphology variants
- CF MΦs fail to control the rough variant compared to smooth

Assani 2017, Assani 2014, Abdulrahman 2011, Hall-Stoodley 2019, Malhotra 2019, Li 2017

Cure CF Columbus (C3) Research Program

- Twice Monthly seminar series
- Translational Core
- Immune Core
- Epithelial Core
- http://www.curecfcolumbus.org/immune.html