
# CAT-5571 AS AN AUTOPHAGY ACTIVATOR THAT ENHANCES THE CLEARANCE OF INTRACELLULAR BACTERIA

40th European Cystic Fibrosis Conference 2017

WS07.6, June 8th, 2017

Feng Liu, Ph.D.

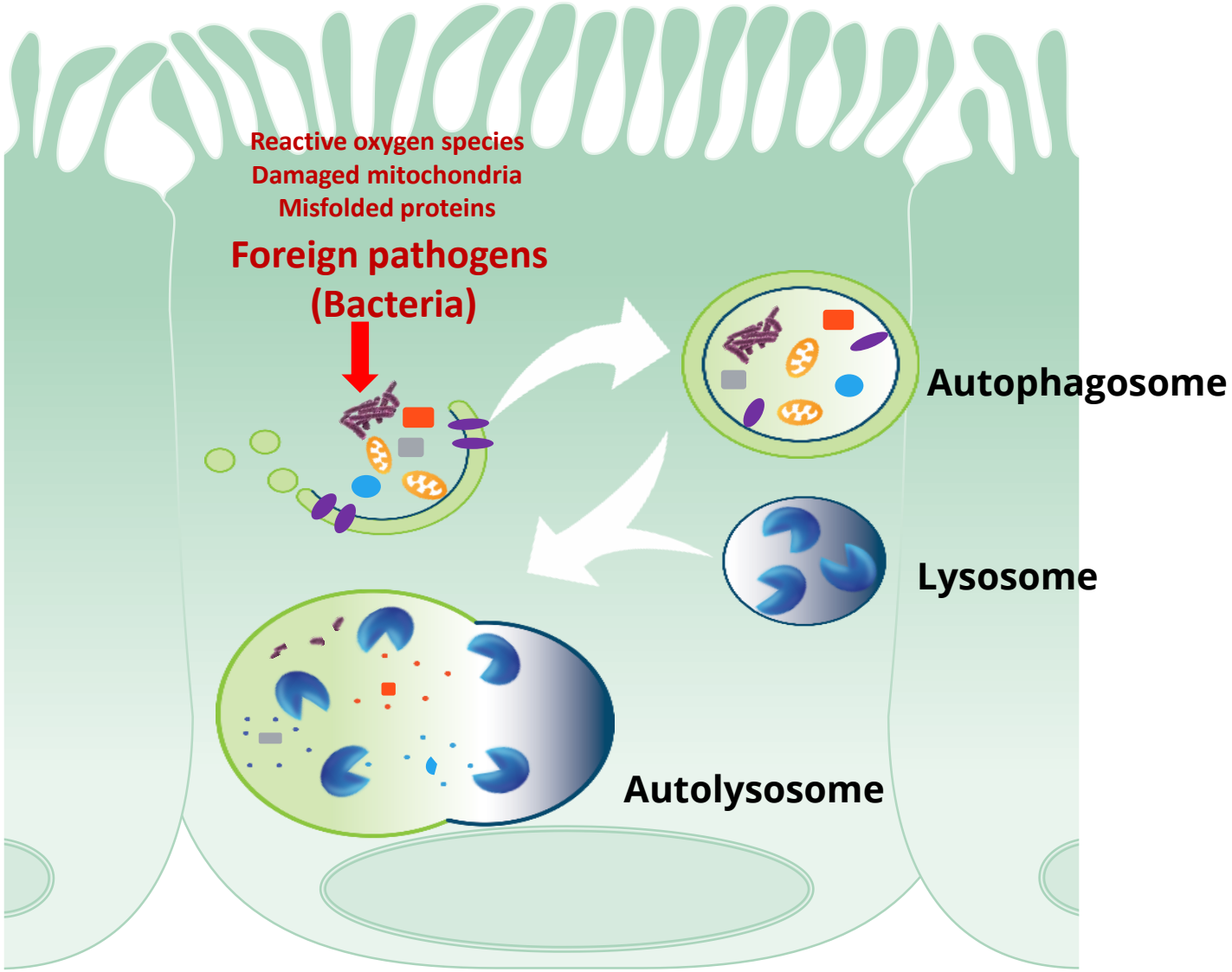
# Forward Looking Statements

**This presentation contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995, including statements regarding our expectations and beliefs about our business, future financial and operating performance, clinical trial plans, product development plans and prospects. The words "believe", "anticipate", "plans," "expect", "could", "should", "will", "would", "may", "intend" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.**

**The forward-looking statements contained in this presentation and in remarks made during this presentation and the following Q&A session are subject to important risks and uncertainties that may cause actual events or results to differ materially from our current expectations and beliefs, including: uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of our product candidates; availability and timing of results from preclinical studies and clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; expectations for regulatory approvals to conduct trials or to market products; availability of funding sufficient for our foreseeable and unforeseeable operating expenses and capital expenditure requirements; other matters that could affect the availability or commercial potential of our product candidates; and general economic and market conditions. These and other risks are described under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the three months ended March 31, 2017, which is on file with the Securities and Exchange Commission, and in other filings that we may make with the Securities and Exchange Commission in the future.**

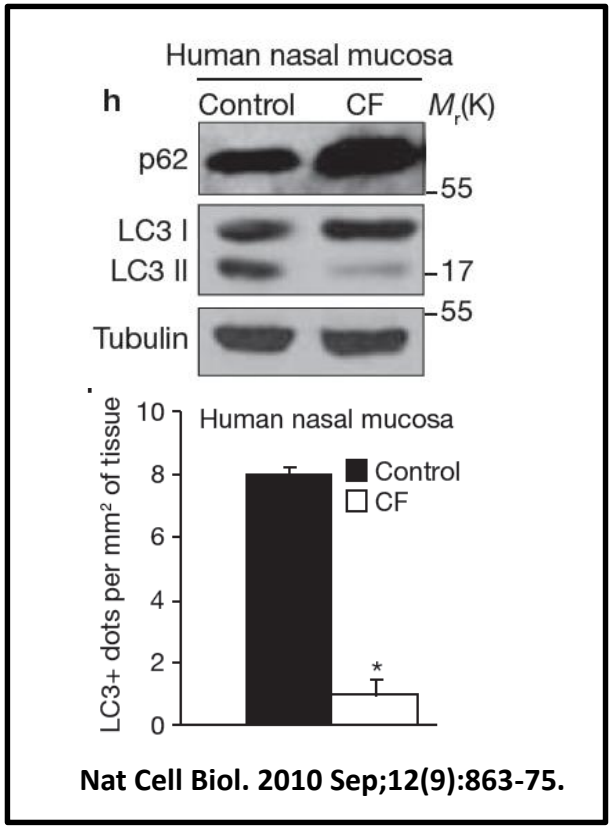
**In addition, the forward-looking statements included in this presentation represent our views as of the date of this presentation. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation.**

# Autophagy: Maintains Cellular Homeostasis and Host Defense

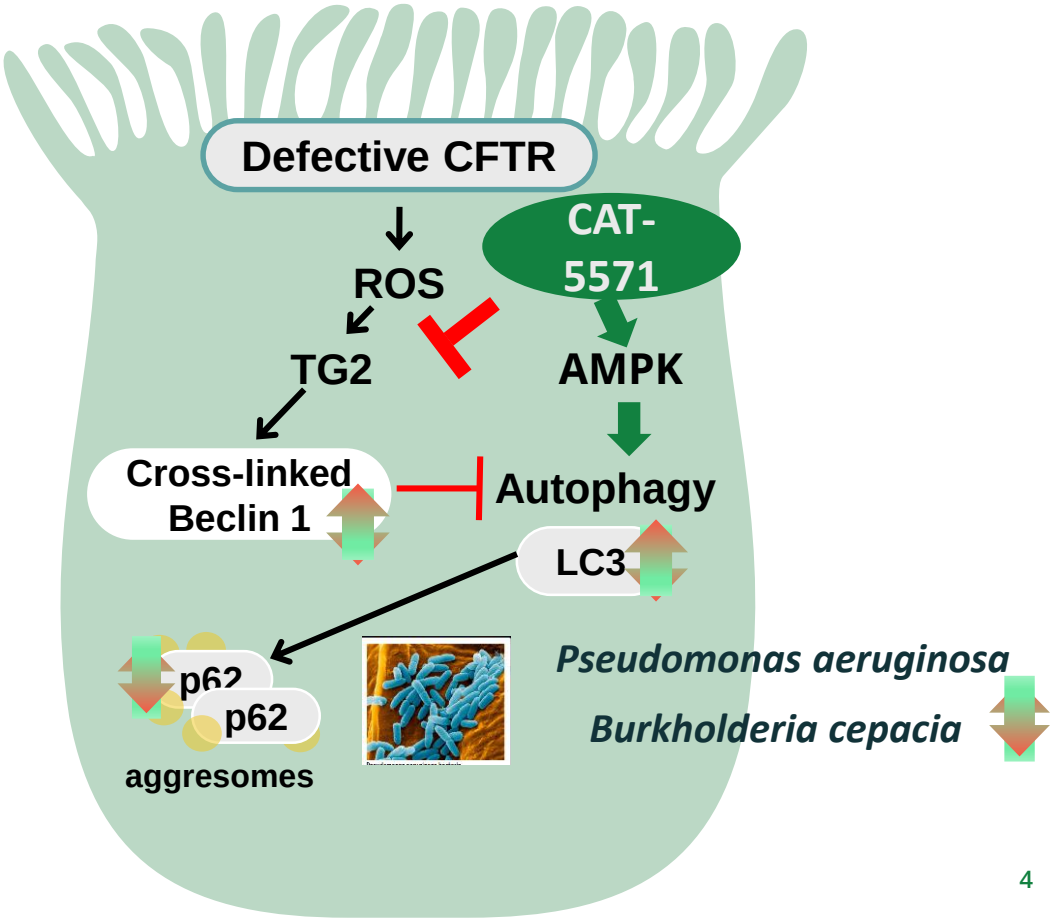


# Autophagy: An Approach to Clear Intracellular Pathogens in CF

## Autophagy is depressed in cystic fibrosis




Nat Cell Biol. 2010 Sep;12(9):863-75.

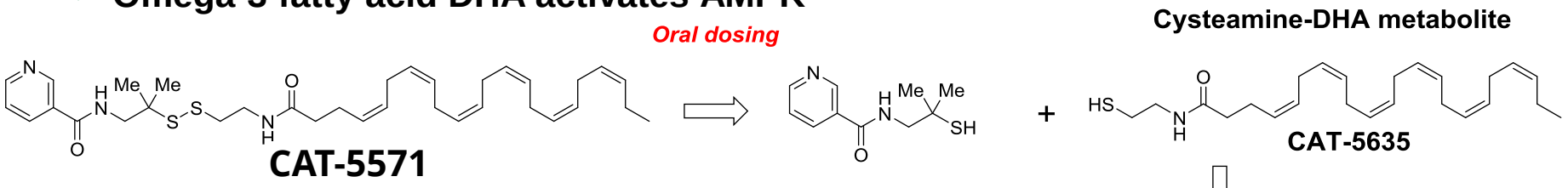


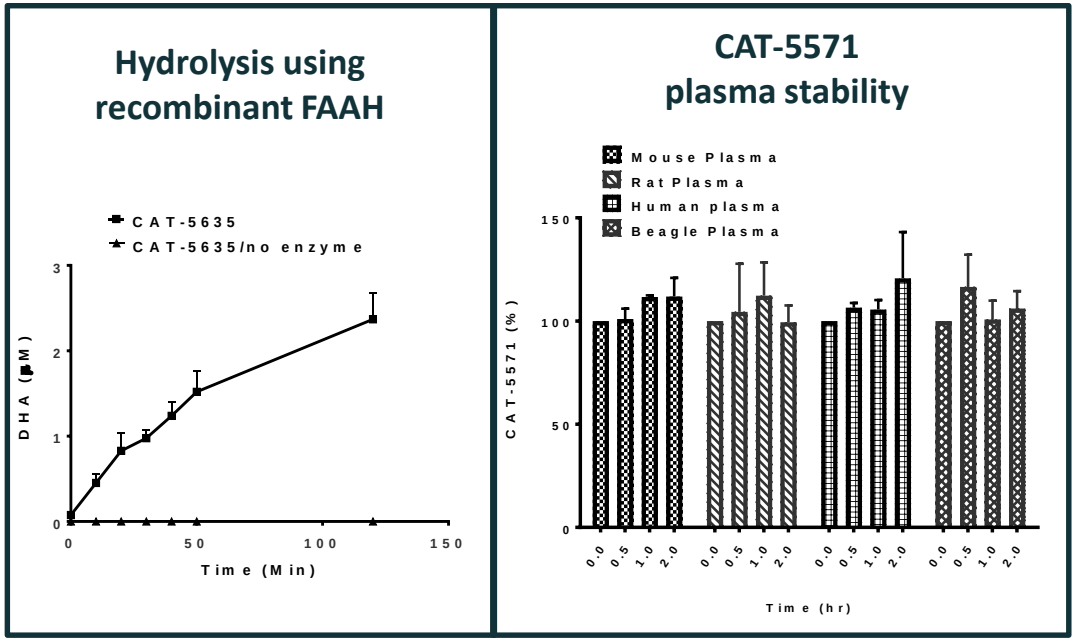



catabasis

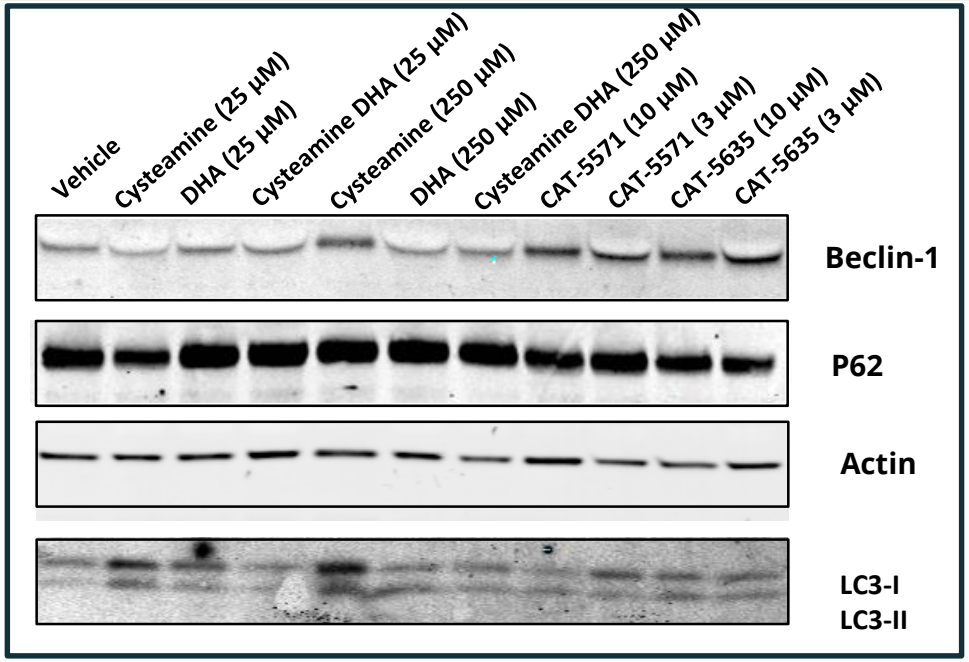
# Discovery of CAT-5571: Application of the SMART Linker Drug Discovery Platform to Activate Autophagy in CF

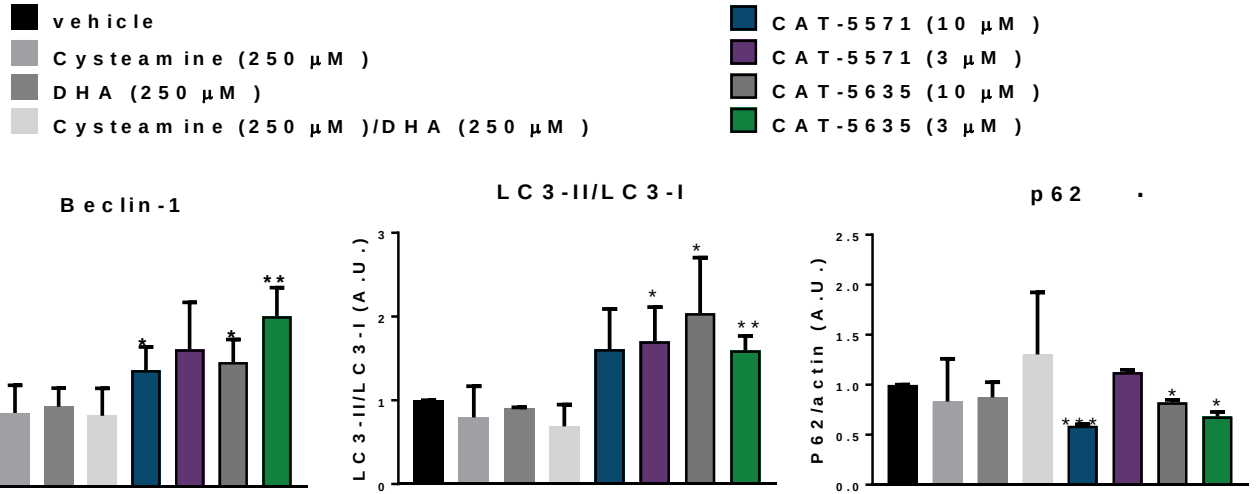
- An approach to activation of autophagy in CF
  - Cysteamine inhibits transglutaminase 2
  - Omega-3 fatty acid DHA activates AMPK



# CAT-5571 Synergistically Activates Autophagy in Human CFTR F508del/F508del hCFBEs

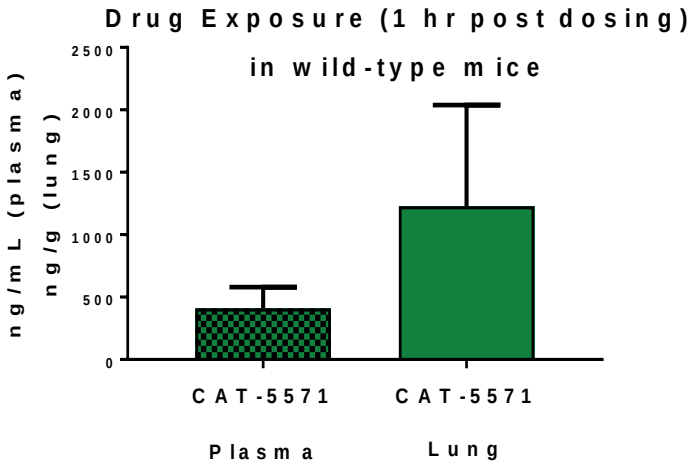


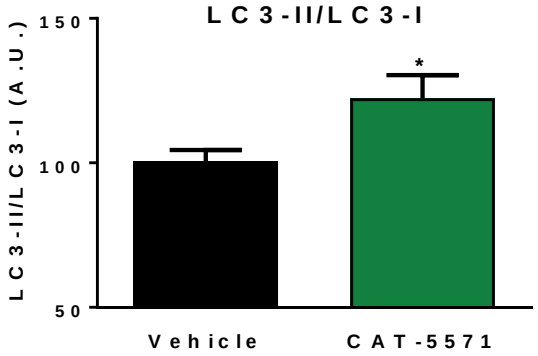




Mean ± SEM mean (n = 3). *p < 0.05 compared to the vehicle, t-test.

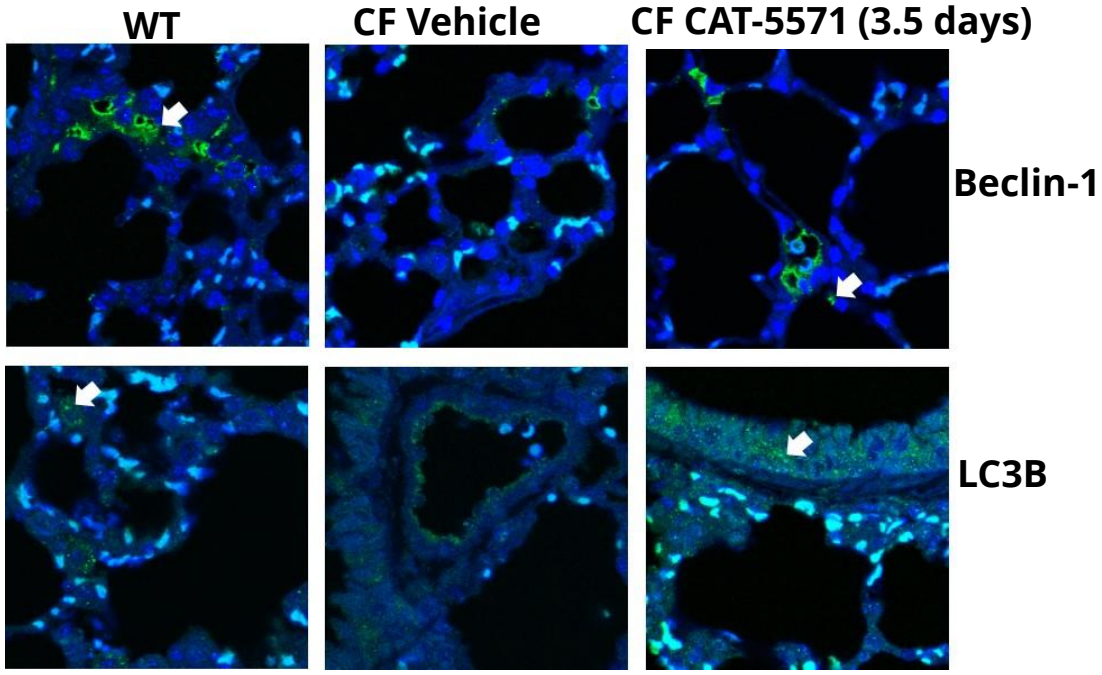
catabasis

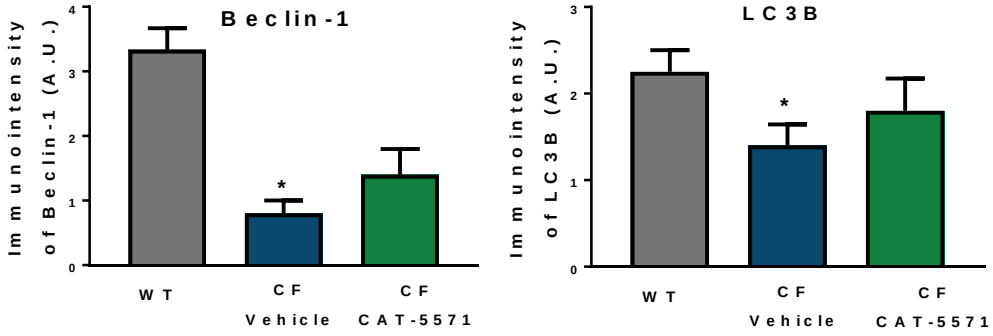
# CAT-5571 Activates Autophagy in the Lung of CFTR F508del/F508del mutant mice



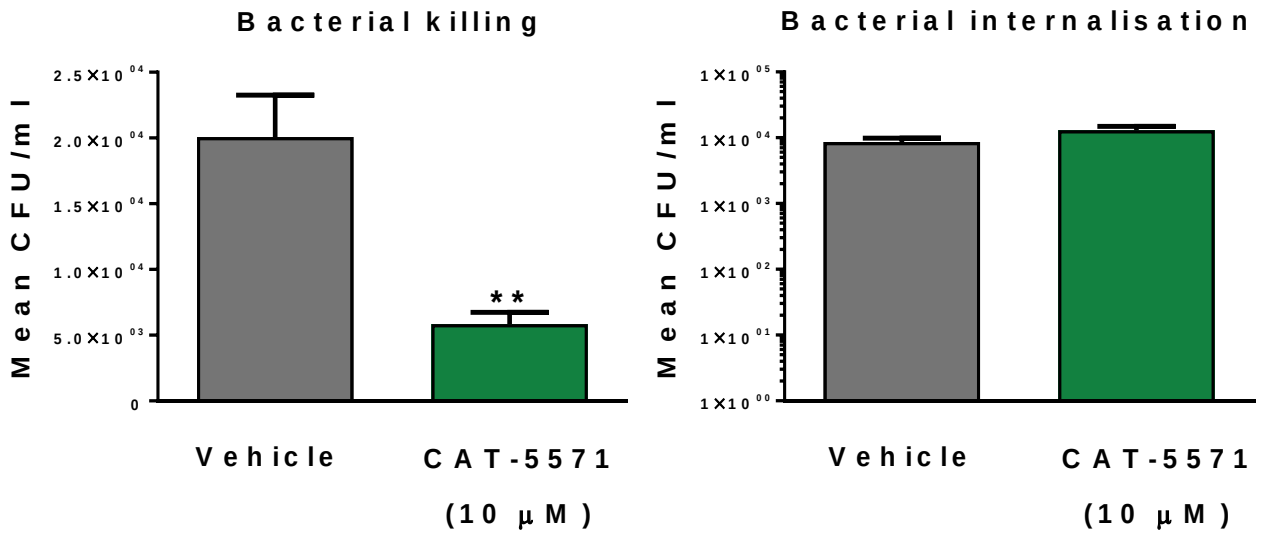

Mean ± SEM mean (n = 16). *p < 0.05 compared to the vehicle, t-test.




Mean ± SEM mean(n = 6). *p < 0.05 compared to the WT, t-test.

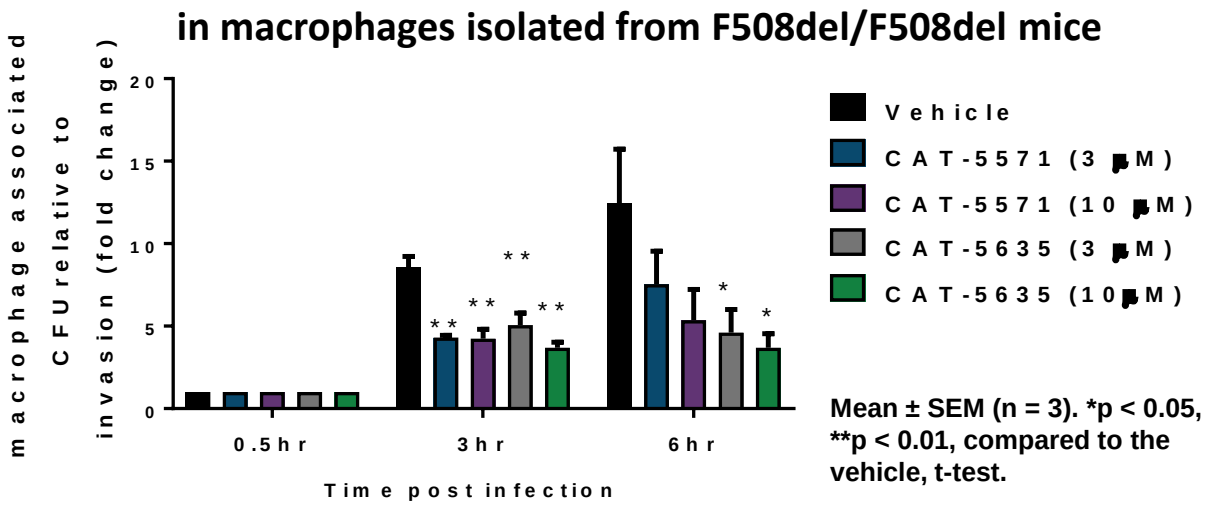
# CAT-5571 Causes a Significant Reduction in the Intracellular *P. aeruginosa* in F508del CF hBEs

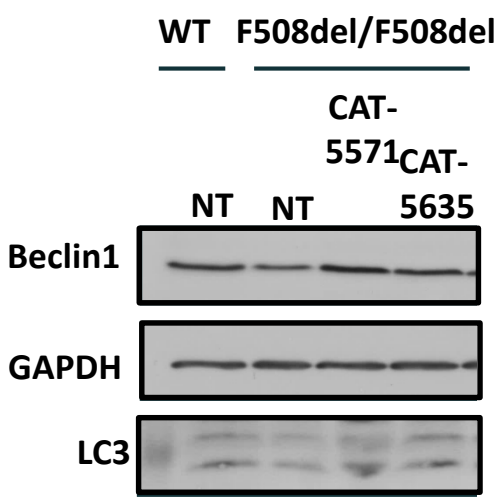


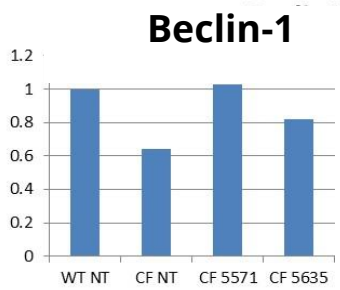

Mean ± SEM, ***p* < 0.01,one-way ANOVA followed by Dunnett's multiple comparison test

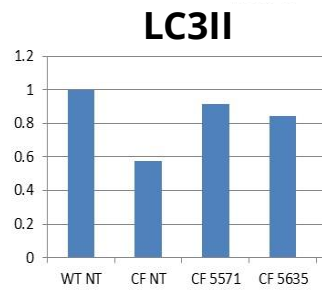
**CAT-5571 is not an antibiotics (MIC against P. aeruginosa > 860 µM)**

# CAT-5571 Causes a Significant Reduction in the Intracellular *B. Cepacia* in Macrophages



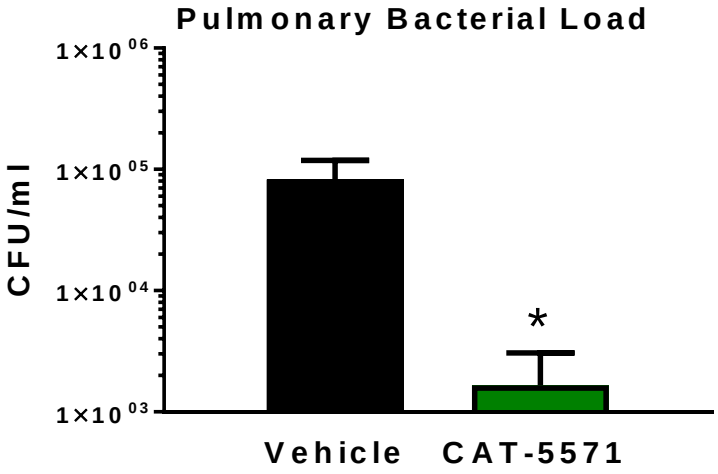



# CAT-5571 Clears Pulmonary Pseudomonas Infection, Reduces Inflammation in F508del/F508del CF Mice

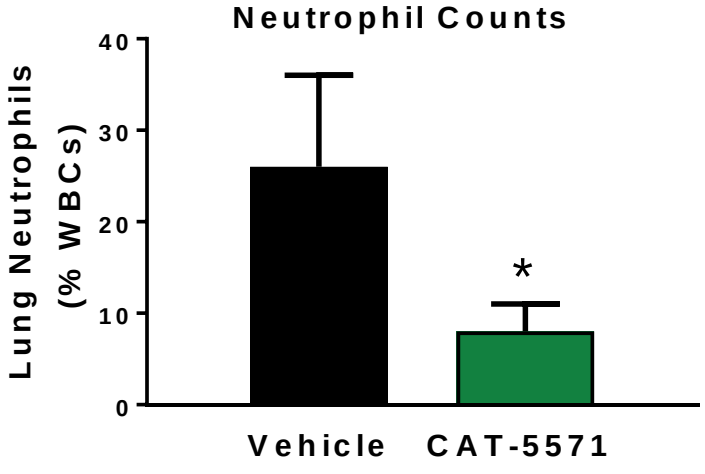
## A chronic bacterial infection model in CF ΔF508/ΔF508 mice

*P. aeruginosa* Infection at day 0, CAT-5571 start at day 1, (100 mg/kg, 9 days, BID, PO)

**Day 10**



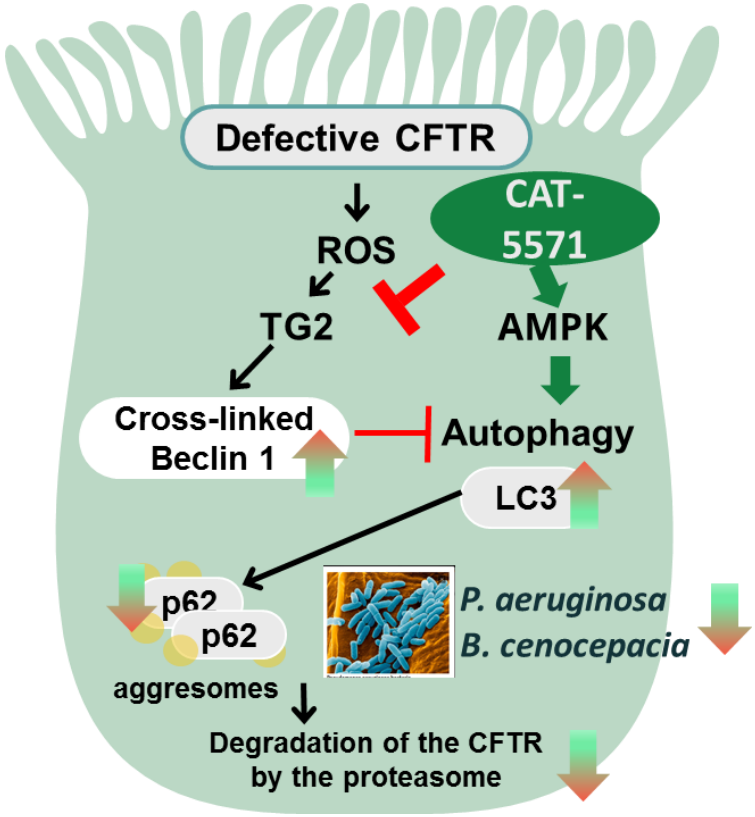

**Day 10**




*p<0.05, utilizing using the analysis of variance between vehicle and CAT-5571 treated animals.

**No exacerbation (No increased bacterial load or neutrophil counts) at day 3 was observed**

# CAT-5571: A Novel Approach to Treatment of CF




**CAT-5571 can significantly enhance CFTR chloride current in combination with ivacaftor/lumacaftor**

**(Vu et al. J Med Chem, 2017. 60(1): p. 458-473.)**

**CAT-5571 represents a potential new therapeutic for improving clinical outcomes in conjunction with current therapies for CF**

# Acknowledgments


- **Catabasis team:**
  - Chi Vu
  - Andy Nichols
  - John Reilly
  - Sachin Chandran
  - Ron Shmueli
  - Diana Lee
  - Dominic Picarella
  - Amal Ting
  - Allison Wensley
  - Derek Wachtel
  - Hanlan Liu
  - Ericka Benson
  - Rafif Dagher
  - Alex Chou
  - Jennifer Kolucki

- **Case Western Reserve University (Cleveland, Ohio):**

  Dr. Tracey Bonfield

  Dr. David Fletcher

- **Ohio State University (Columbus, Ohio)**

  Dr. Amal Amer

  Dr. Kathrin Krause

- **KWS BioTest (Bristol, UK)**

  Dr. Claire Richards