UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of
The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): March 13, 2017

CORBUS PHARMACEUTICALS HOLDINGS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**000-55327**	**46-4348039**
(State or other jurisdiction of incorporation)	*(Commission File Number)*	*(IRS Employer Identification No.)*

100 River Ridge Drive, Norwood, MA	**02062**
(Address of principal executive offices)	*(Zip Code)*

Registrant's telephone number, including area code: **(617) 963-0100**

Not Applicable
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

[ ] Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

[ ] Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

[ ] Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

[ ] Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 7.01. Regulation FD Disclosure.

On March 13, 2017, Corbus Pharmaceuticals Holdings, Inc. (the "Company") used the slides attached hereto as Exhibit 99.1 in connection with management presentations to describe its business.

The information in this Current Report on Form 8-K under Item 7.01, including the information contained in Exhibit 99.1, is being furnished to the Securities and Exchange Commission, and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934 or otherwise subject to the liabilities of that section, and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933 or the Securities Exchange Act of 1934, except as shall be expressly set forth by a specific reference in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) The following exhibit is furnished with this report:

Exhibit No.	Description
99.1	Investor Presentation.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

CORBUS PHARMACEUTICALS HOLDINGS, INC.

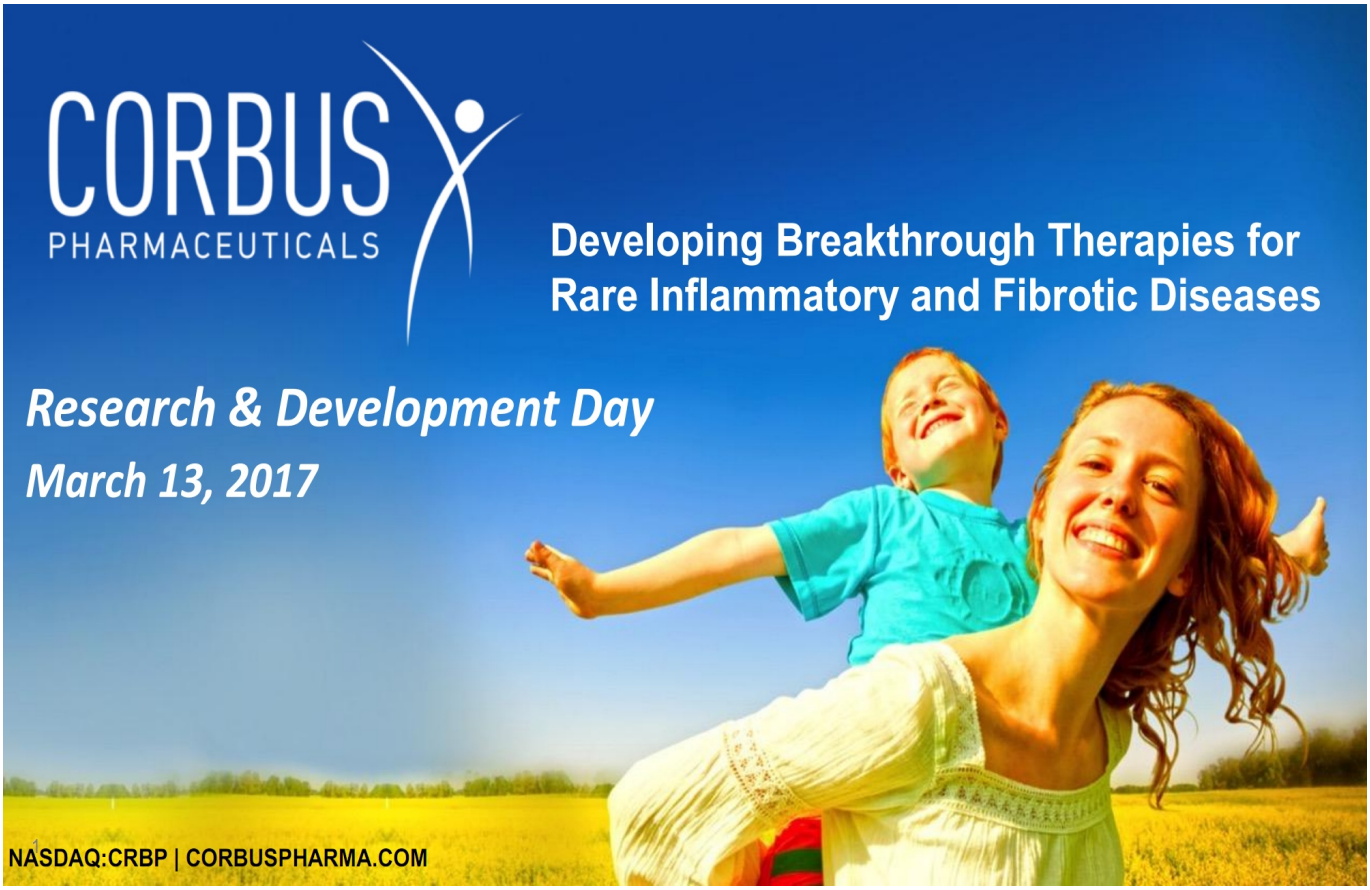
Dated: March 13, 2017

By: */s/ Yuval Cohen*
Name: Yuval Cohen
Title: Chief Executive Officer

EXHIBIT INDEX

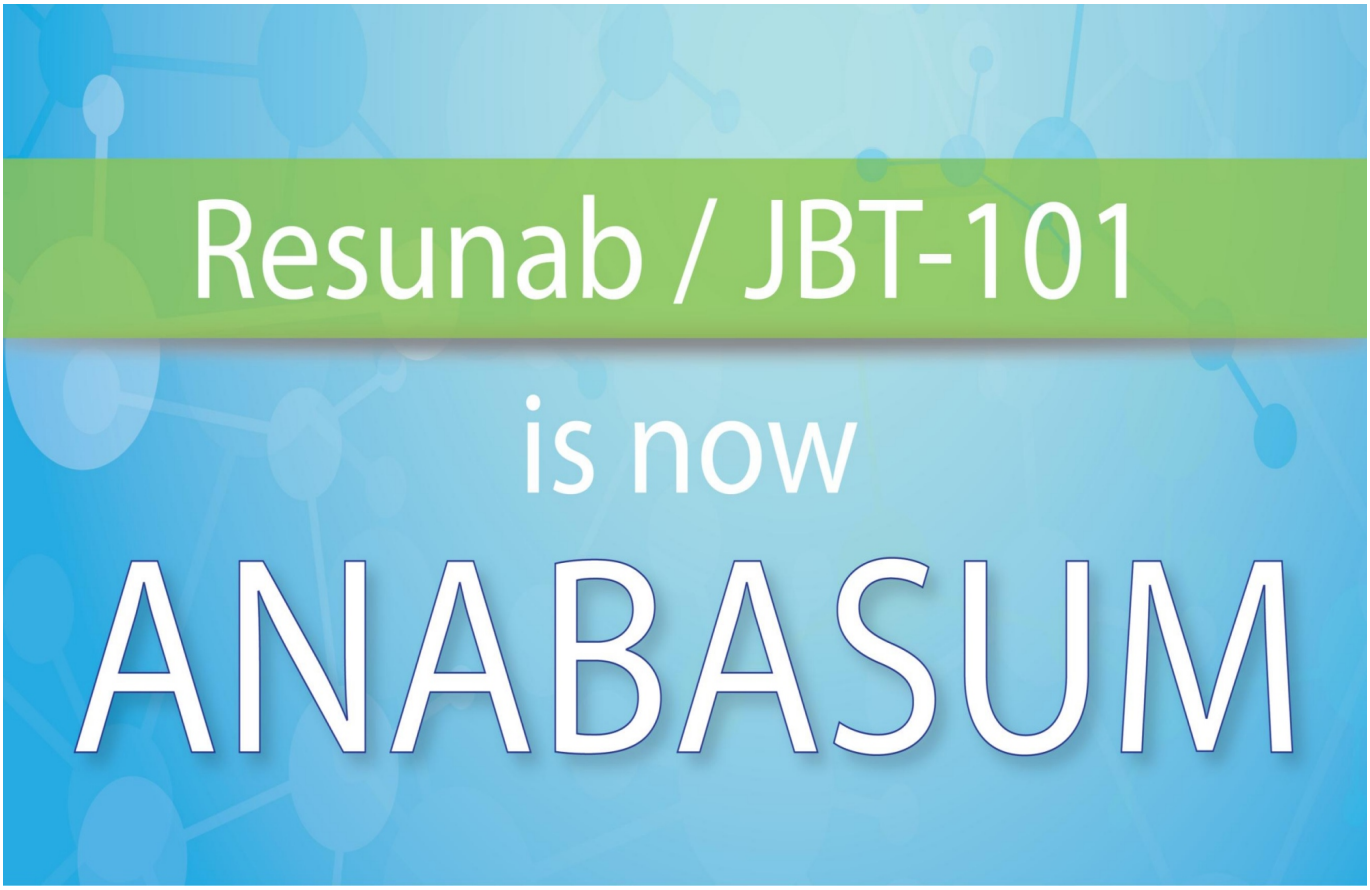
Exhibit No.	Description
99.1	Investor Presentation.

Exhibit 99.1


CORBUS
PHARMACEUTICALS
Developing Breakthrough Therapies for
Rare Inflammatory and Fibrotic Diseases
Research & Development Day
March 13, 2017
NASDAQ:CRBP | CORBUSPHARMA.COM

FORWARD-LOOKING STATEMENTS

This presentation contains certain forward-looking statements, including those relating to the Company's product development, clinical trials, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statements that are predictive in nature. Additional written and oral forward-looking statements may be made by the Company from time to time in filings with the Securities and Exchange Commission (SEC) or otherwise. The Private Securities Litigation Reform Act of 1995 provides a safe-harbor for forward-looking statements. These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the SEC. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this presentation. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.


Resunab / JBT-101
is now
ANABASUM

AGENDA

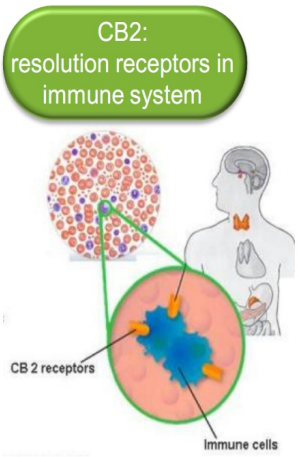
- **Introduction**
  - Yuval Cohen, Ph.D. – Chief Executive Officer
- **Anabasum: Background, MOA and Updates**
  - Barbara White, M.D. – Chief Medical Officer
- **Systemic Sclerosis Phase 2 Study: Gene Expression Patterns**
  - Michael L. Whitfield, Ph.D. – Professor, Department of Molecular and Systems Biology, Director of Quantitative Biomedical Sciences, Geisel School of Medicine at Dartmouth and Scientific Founder, Celdara Medical, LLC.
- **Human Blister Model: MOA in a Clinical Model of Inflammation/Resolution**
  - Derek Gilroy, Ph.D. – Head, Centre for Clinical Pharmacology and Professor of Immunology at Queen Mary College, University College London
- **Cystic Fibrosis: Biochemistry of Inflammation and *Ex-Vivo* Lung Macrophage Data**
  - Michael Knowles, M.D. – Professor of Pulmonary and Critical Care Medicine at University of North Carolina Chapel Hill and member of the Company's Scientific Advisory Board, and expert in inflammation in CF
- **Cystic Fibrosis Phase 2 Study: Role of Inflammation, Protocol, Study Design and Outlook**
  - James Chmiel, M.D., M.P.H. – Professor of Pediatrics, Case Western Reserve University, Associate Director of the LeRoy W. Matthews Cystic Fibrosis Center at University Hospitals Rainbow Babies and Children's Hospital in Cleveland, and Principle Investigator of the Company's Phase 2 cystic fibrosis clinical study
- **Closing Remarks**
  - Yuval Cohen, Ph.D. – Chief Executive Officer

Anabasum: Background, MOA and Updates

Barbara White M.D.
Chief Medical Officer

ANABASUM

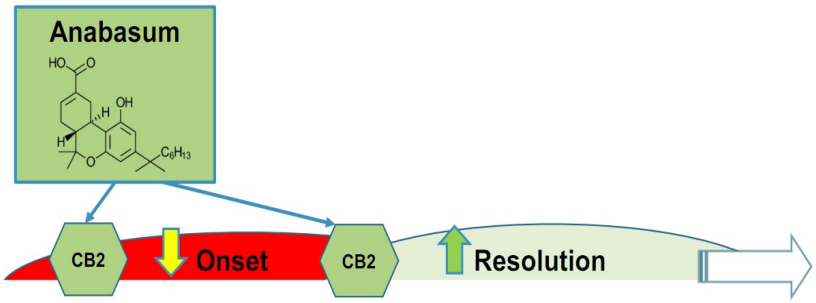
- First selective cannabinoid receptor type 2 (CB2) agonist to target inflammatory and fibrotic diseases
- Synthetic small molecule with oral dosing



CB2

- Receptor in immune and endocannabinoid systems
- Preferentially expressed on immune cells
- Expressed following cellular activation
- Triggers **resolution** of innate immune responses
- Surface expression returns to low basal levels when resolution is complete

ANABASUM SHIFTS THE BALANCE FROM ONSET PHASE TO RESOLUTION PHASE OF INNATE IMMUNE RESPONSES



HOMEOSTASIS: RESOLUTION of

- **Infection**
- **Inflammation**
- **Fibrosis**

Anabasum is not immunosuppressive

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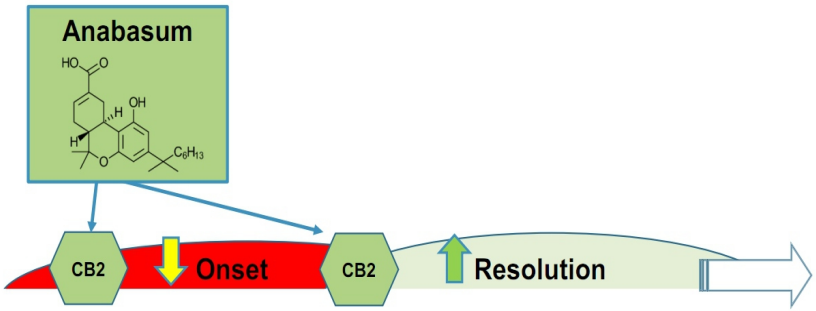
MICHAEL WHITFIELD: GENE EXPRESSION CHANGES IN SKIN BIOPSIES FROM ANABASUM PHASE 2 SYSTEMIC SCLEROSIS TRIAL



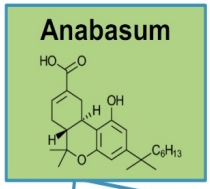
- Pro-inflammatory lipids
- Vasodilation/ edema
- Chemokines
- Tissue infiltration with neutrophils and other inflammatory cells
- Pro-inflammatory cytokines
- Vascular growth factors
- Pro-fibrotic growth factors
- Extracellular matrix production

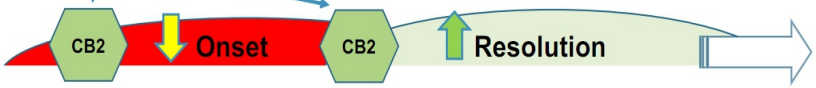
- Pro-resolving lipid mediators
- Pro-resolving macrophages
- Clearance of bacteria
- Resolution of tissue infiltration with inflammatory cells

HOMEOSTASIS: RESOLUTION of

- **Infection**
- **Inflammation**
- **Fibrosis**

DEREK GILROY: ANABASUM REDUCES ONSET AND SPEEDS RESOLUTION IN A HUMAN MODEL OF INFECTION-INDUCED INNATE IMMUNE RESPONSE





- Pro-inflammatory lipids
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HOMEOSTASIS: RESOLUTION of

- **Infection**
- **Inflammation**
- **Fibrosis**

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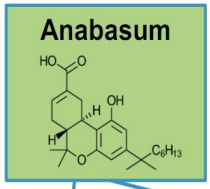
MICHAEL KNOWLES: ANABASUM REDUCES "INFECTION"-INDUCED INNATE IMMUNE RESPONSES BY HUMAN CYSTIC FIBROSIS ALVEOLAR MACROPHAGES



CB2 **Onset** CB2 **Resolution**

- Pro-inflammatory lipids
- Vasodilation/ edema
- Chemokines
- Tissue infiltration with neutrophils and other inflammatory cells
- Pro-inflammatory cytokines
- Vascular growth factors
- Pro-fibrotic growth factors
- Extracellular matrix production

- Pro-resolving lipid mediators
- Pro-resolving macrophages
- Clearance of bacteria
- Resolution of tissue infiltration with inflammatory cells

HOMEOSTASIS: RESOLUTION of

- **Infection**
- **Inflammation**
- **Fibrosis**

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JAMES CHMIEL: IMPORTANCE OF INFLAMMATION IN CYSTIC FIBROSIS

Pathologic processes of unresolved
- **Infection**
- **Inflammation**
- **Fibrosis**

One or more are essential to tissue damage and organ dysfunction in

- **Systemic sclerosis**: next steps in development program following end-of-Phase 2 meeting with FDA – March 2017
- **Cystic fibrosis**: data from Phase 2 study – March 2017
- **Dermatomyositis**: data from Phase 2 study – summer 2017
- **Systemic lupus erythematosus**: Phase 2 study start – 2Q17

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Systemic Sclerosis Phase 2 Study: Gene Expression Patterns

EFFECT OF ANABASUM ON GENE EXPRESSION IN SKIN BIOPSIES FROM SYSTEMIC SCLEROSIS PATIENTS IN THE JBT101-SSc-001 STUDY

Michael L. Whitfield, Ph.D.

Professor, Department of Molecular and Systems Biology, Director of Quantitative Biomedical Sciences, Geisel School of Medicine at Dartmouth and Scientific Founder, Celdara Medical, LLC.

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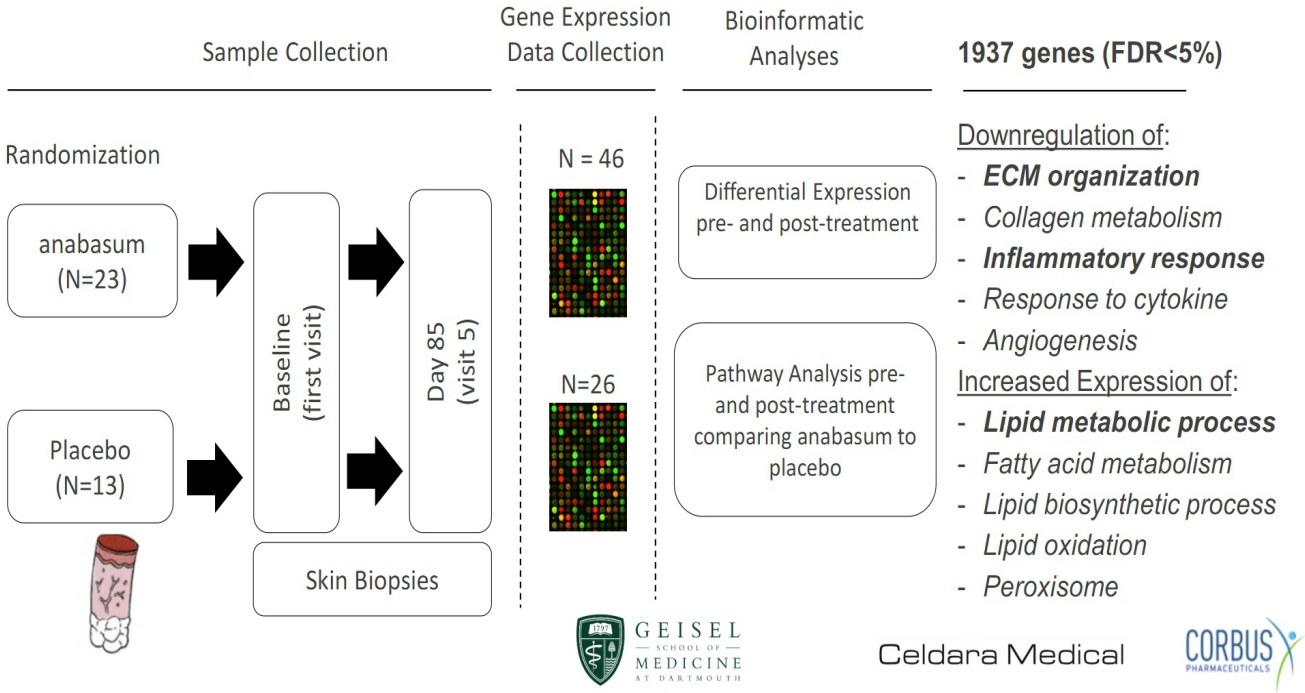
SUMMARY

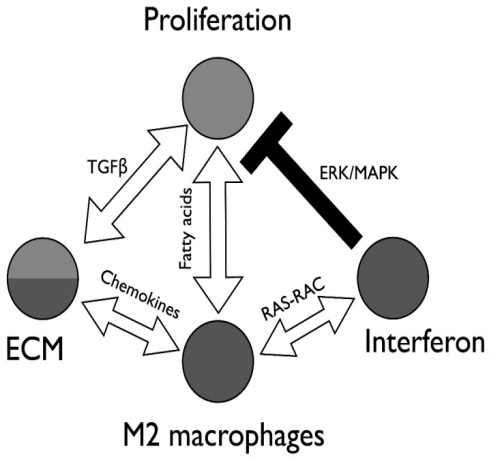
- Anabasum effects are clearly seen in short term gene expression studies, with significant differences between anabasum and placebo arms
- Anabasum is hitting pathways thought to be of high importance to SSc. Three representative pathways, each highly relevant to SSc, are modulated by anabasum
  - Extracellular matrix-related genes decrease expression with treatment
  - Inflammation-related genes decrease expression with treatment
  - Lipid metabolism genes increase expression with treatment
- These quantitative gene expression data corroborate evidence of clinical benefit in the trial, as does results from a quantitative modified Rodnan skin score surrogate test.

APPROACH TO AND RESULTS OF ANALYSES OF GENE EXPRESSION IN SKIN BIOPSIES FROM SUBJETCS WITH SYSTEMIC SCLEROSIS TREATED WITH ANABASUM AND PLACEBO



INFLAMMATION IS A KEY DRIVER OF TISSUE DAMAGE IN SYSTEMIC SCLEROSIS

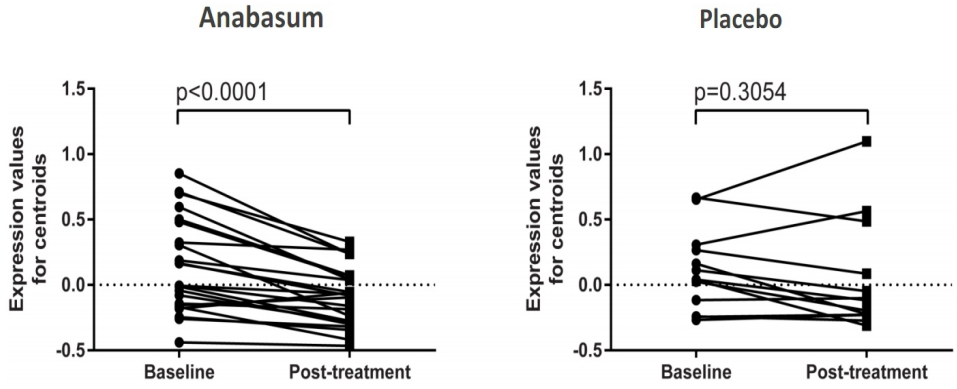
- Inflammation is associated with active SSc (reviewed in Johnson et al. 2015 Seminars Immunopathology)
- Most therapies that have impacted SSc clinically target the immune system (Taroni et al. 2016 J. Invest Derm.)
  - None are FDA-approved for treatment of SSc
- SSc risk polymorphisms fall into immune genes (Mahoney et al. 2015 PLoS Comp Biol)
- An immune – fibrosis link is a common feature of all affected organs analyzed (Taroni et al. Genome Medicine 2017, *In Press*)



Adapted from Mahoney et al. 2015 PLoS Comp Biol

ANABASUM TREATMENT SIGNIFICANTLY INHIBITS EXPRESSSION OF *INFLAMMATORY RESPONSE* GENES

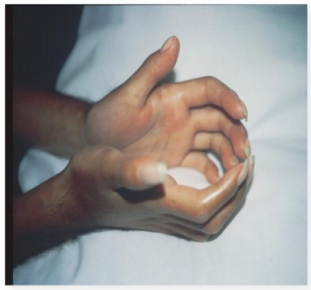
Average expression per patient of 47 genes that map to the *Inflammatory Response* pathway
(example genes include CCL1, CCL2, CCL5, CXCL10, IL4R, ICAM1, multiple interferon-induced genes, and TLR9)

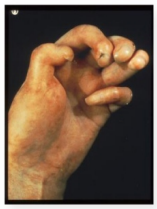


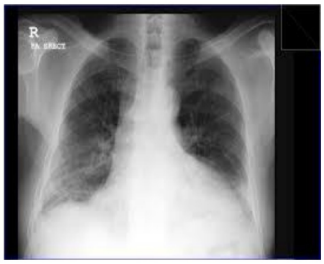
p-values calculated by paired t-test

EXCESSIVE EXTRACELLULAR MATRIX DEPOSITION (FIBROSIS) IS A HALLMARK OF TISSUE DAMAGE IN SYSTEMIC SCLEROSIS

- Increased expression of extracellular matrix (ECM) genes causes skin and internal organ fibrosis in SSc (Bhattacharyya et al. Nat. Rev Rheumatol. 2011)
- Progressive organ fibrosis and vascular damage results in chronic morbidity and high mortality in SSc (Allanore et al. Nat. Rev Dis Primers 2015)
- No FDA-approved therapies to stop the process of fibrosis in SSc (Denton, Clin. Exp. Rheumatol 2015)







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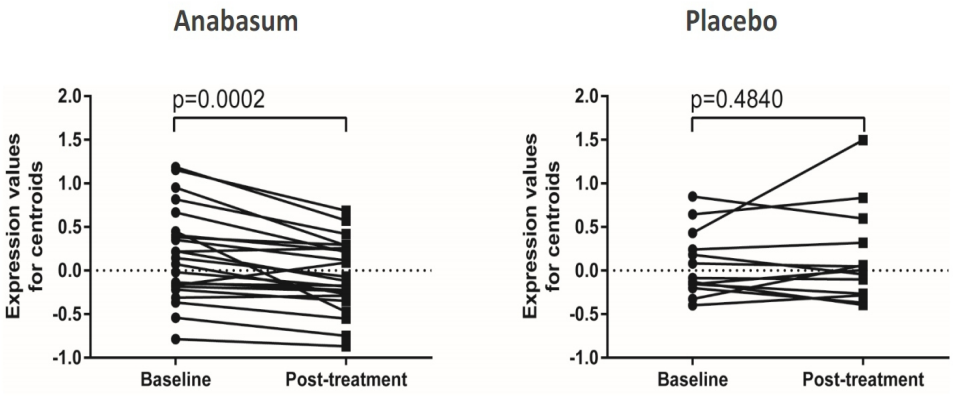
ANABASUM TREATMENT SIGNIFICANTLY INHIBITS EXPRESSSION OF *EXTRACELLULAR MATRIX* PATHWAY GENES

Average expression of 35 genes that map to the ECM pathway on a per patient basis
(example genes include TGFβ, CTGF, collagens, fibronectin, tenascin, decorins, thrombospondin 1, SERPINE1)



p-values calculated by paired t-test

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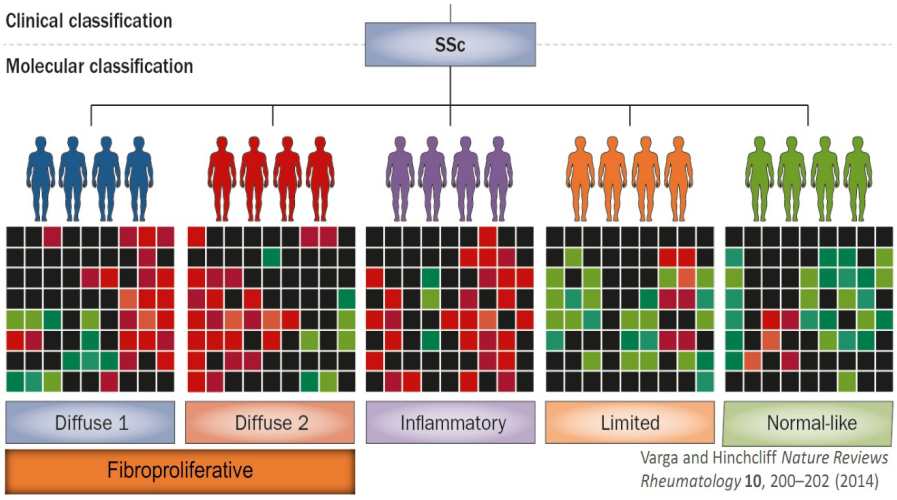
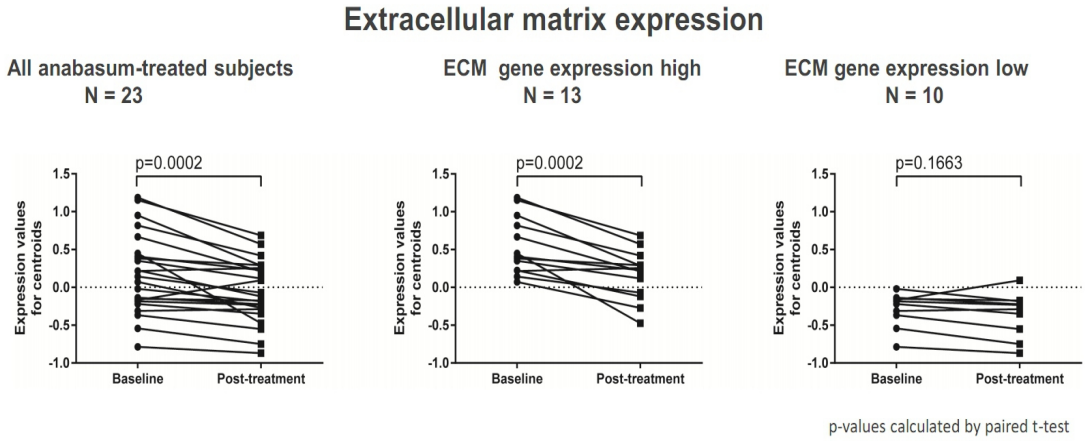
GENE EXPRESSION IN SYSTEMIC SCLEROSIS SKIN IS DOMINATED BY SUBSETS OF "INTRINISIC" GENE EXPRESSION



Varga and Hinchcliff *Nature Reviews Rheumatology* **10**, 200–202 (2014)

- Subsets based on gene expression profiling in skin
- Reproducible in four independent cohorts and across tissues (Milano et al. *PLoS ONE* (2008); Pendergrass et al. *J. Invest. Dermatol.* (2012); Hinchcliff et al. *J. Invest. Dermatol.* (2013); Johnson et al. *PLoS ONE* (2015); Mahoney et al. *PLoS Comp Biol* (2015); Taroni et al. *Arthritis Res. Therapy* (2015); Taroni et al. *Genome Medicine* (2017), *in press*

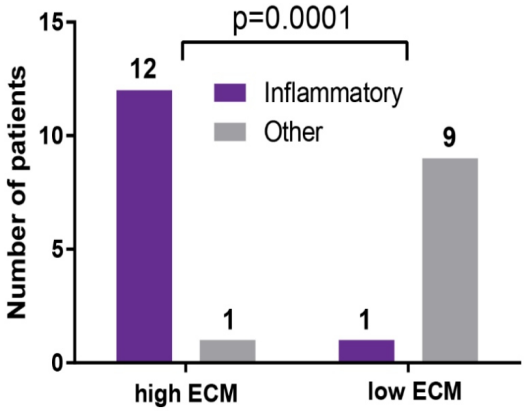
HIGH EXPRESSION OF THE ECM PATHWAY OCCURS IN SUBJECTS WHOSE GENE EXPRESSION IN SKIN FALLS WITHIN THE INTRINISIC INFLAMMATORY SUBSET



p-values calculated by paired t-test

- Decrease in ECM gene expression in anabasum-treated subjects is preferentially driven by patients with high baseline ECM gene expression

HIGH EXPRESSION OF THE ECM PATHWAY OCCURS IN PATIENTS WHOSE GENE EXPRESSION IN SKIN FALLS WITHIN THE INTRINISIC INFLAMMATORY SUBSET



Fisher's exact test

- Findings are consistent with inflammation driving fibrosis in SSc

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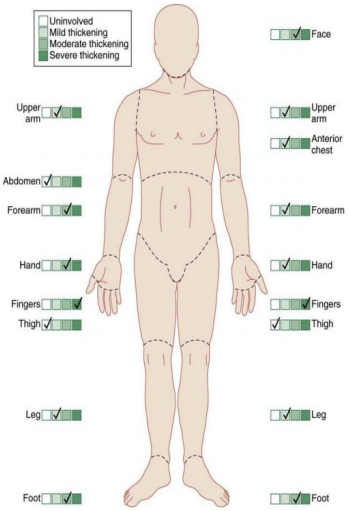
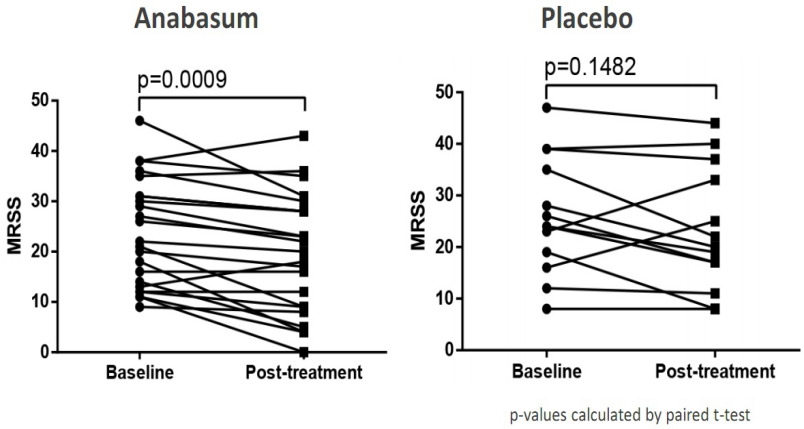
ANABASUM-INDUCED CHANGES IN THE MODIFIED RODNAN SKIN SCORE, A CLINICAL MEASURE OF SKIN FIBROSIS, PARALLEL THE MOLECULAR CHANGES

- Pinch test at 17 sites across the body
- Standard outcome measure





p-values calculated by paired t-test

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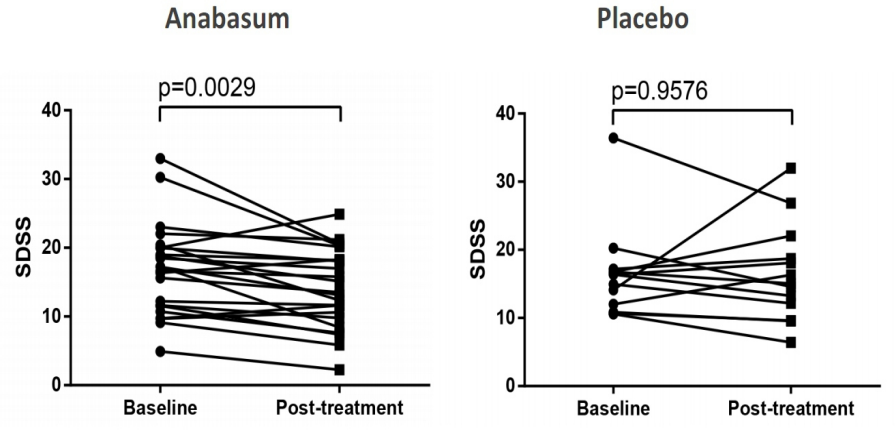
SCLERODERMA DISEASE SEVERITY SCORE (SDSS) IS A QUANTITATIVE MODIFIED RODNAN SKIN SCORE SURROGATE CALCULATED FROM GENE EXPRESSION IN SKIN BIOPSIES

This mathematical model was developed and tested on hundreds of SSc skin biopsy samples with corresponding mRSS score measured concurrently by the same physician

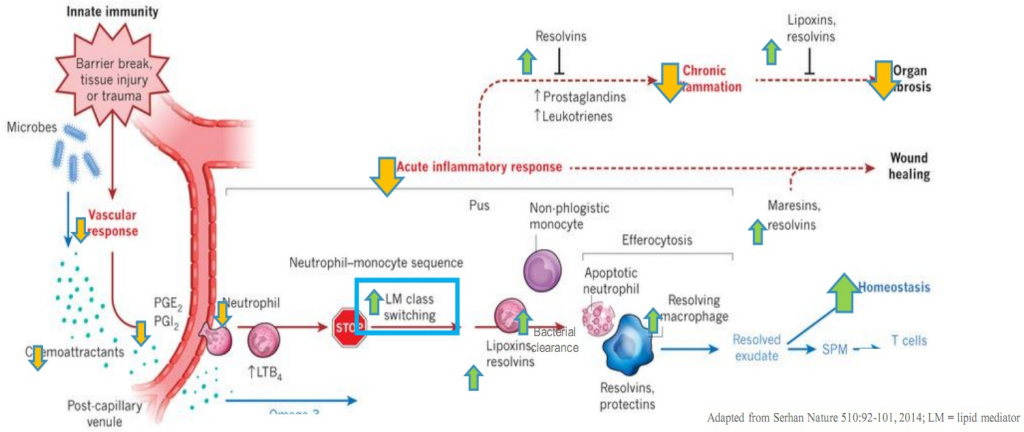
- Calculated from the expression level of a subset of specific genes from the genomic DNA microarray data
- Validated on five independent SSc patient cohorts
- Highly correlated with mRSS (R = 0.8); not subject to inter- or intra-observer variability

ANABASUM TREATMENT SIGNIFICANTLY DECREASES SCLERODERMA DISEASE SEVERITY SCORE



p-values calculated by paired t-test

ANABASUM'S MECHANISM OF ACTION INCLUDES CLASS SWITCH FROM PRO-INFLAMMATORY TO PRO-RESOLVING LIPD MEDIATORS

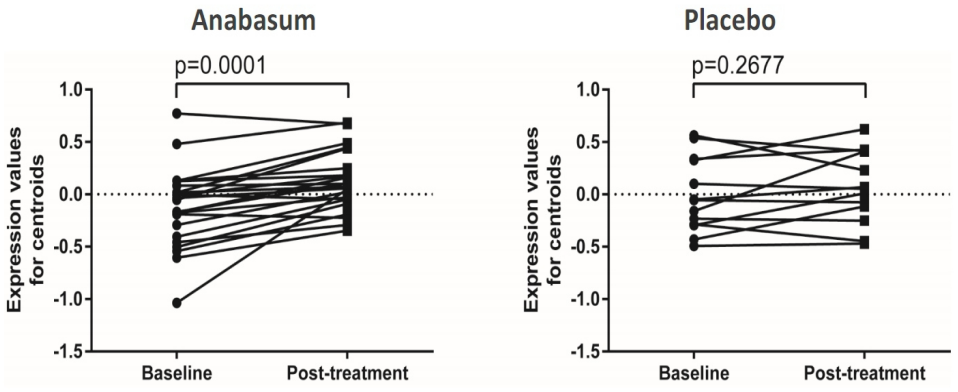


Adapted from Serhan Nature 510:92-101, 2014; LM = lipid mediator

- Class switch of lipid mediators from pro-inflammatory to pro-resolving is the upstream event in initiation of resolution phase of innate immune responses and has been observed with anabasum exposure
  - Animal models – increase lipoxin A4 and PDJ2
  - Healthy human volunteers - shift from pro-inflammatory to pro-resolving lipid mediators
  - SSc patients in JBT101-SSc-001 Phase 2 study – increase in 17HDHA and D series resolvins versus decrease in 5-HETE, 15-HETE, and 15-HEPE

ANABASUM TREATMENT SIGNIFICANTLY INCREASES LIPID METABOLISM PATHWAY GENES IN SKIN BIOPSIES FROM SYSTEMIC SCLEROSIS PATIENTS

Average expression per patient of 142 genes in the *Lipid Metabolism* pathway
(example genes include acetoacetyl-Coa synthetase, fatty acid synthase, multiple fatty acid binding proteins, desaturases, and hydrolases, insulin induced gene 1, and SIRT1)



p-values calculated by paired t-test

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CONCLUSIONS

- Anabasum induces significant and biologically sensible molecular responses in skin biopsies from systemic sclerosis patients, consistent with resolution of innate immune responses
- Anabasum, but not placebo, significantly increases lipid metabolic process pathways and decreases expression of ECM and Inflammatory Response pathways
  - This includes directionally correct changes in expression of multiple genes known to be important in SSc
- Longer exposure to anabasum may increase gene expression effects

ACKNOWLEDGMENTS

- Celdara Medical, LLC
  - Yolanda Nesbeth, PhD
  - Jake Reder, PhD (CEO)

- Geisel School of Medicine at Dartmouth
  - Michael L. Whitfield, PhD
  - Viktor Martyanov, PhD
  - Guoshuai Cai, PhD
  - Tammara Wood, MS

Q&A

Human Blister Model: MOA in a Clinical Model of Inflammation/Resolution

Derek Gilroy, Ph.D.

Head, Centre for Clinical Pharmacology and Professor of Immunology at Queen Mary College, University College London, and expert in resolution of inflammation

Queen Mary
University of London

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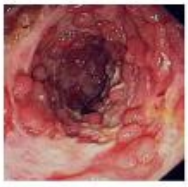
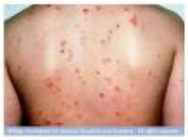
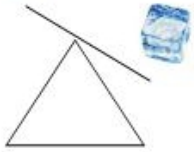
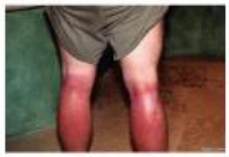
INFLAMMATION









TREATMENTS FOR CHRONIC INFLAMMATORY DISEASES

NSAIDs

Steroids

DMARDs

Biologics

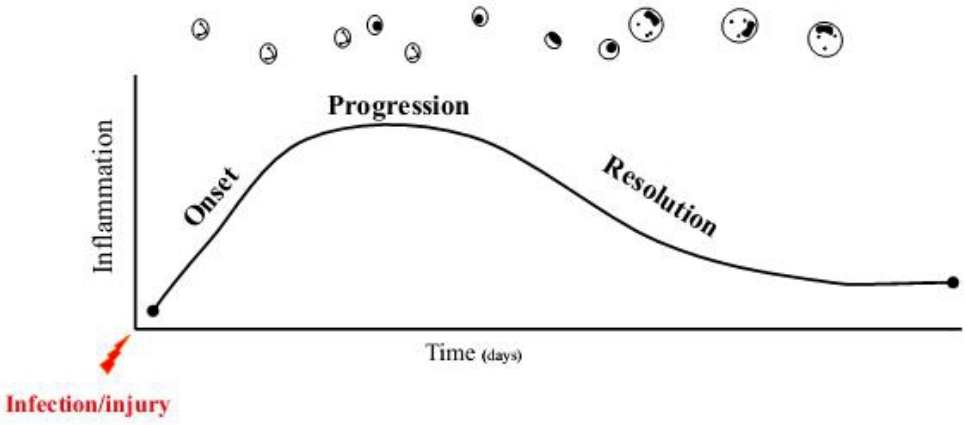
Problem

While they alleviate symptoms….

Side effects

Do not cure underlying disease

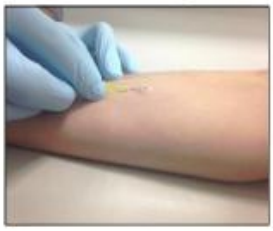
ACUTE INFLAMMATION



- Resolution is an **active** process
- Failure of resolution may predispose to chronic inflammation & tissue injury

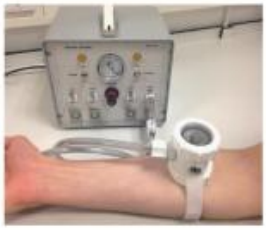
THE MODEL: UV-KILLED E. COLI INDUCED LOCAL INFLAMMATION

I.D. Bacteria Injection

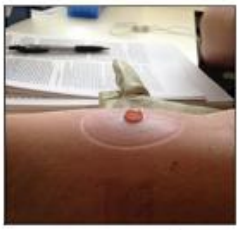


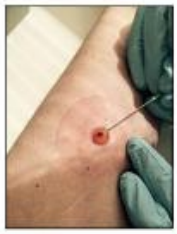
Laser Doppler Imager

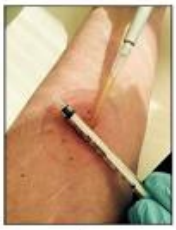
Blister Induction



Blister Fluid Aspiration







The Journal of Pathology: Clinical Research
J Path: Clin Res July 2016; 2: 154–165
Published online 16 March 2016 in Wiley Online Library

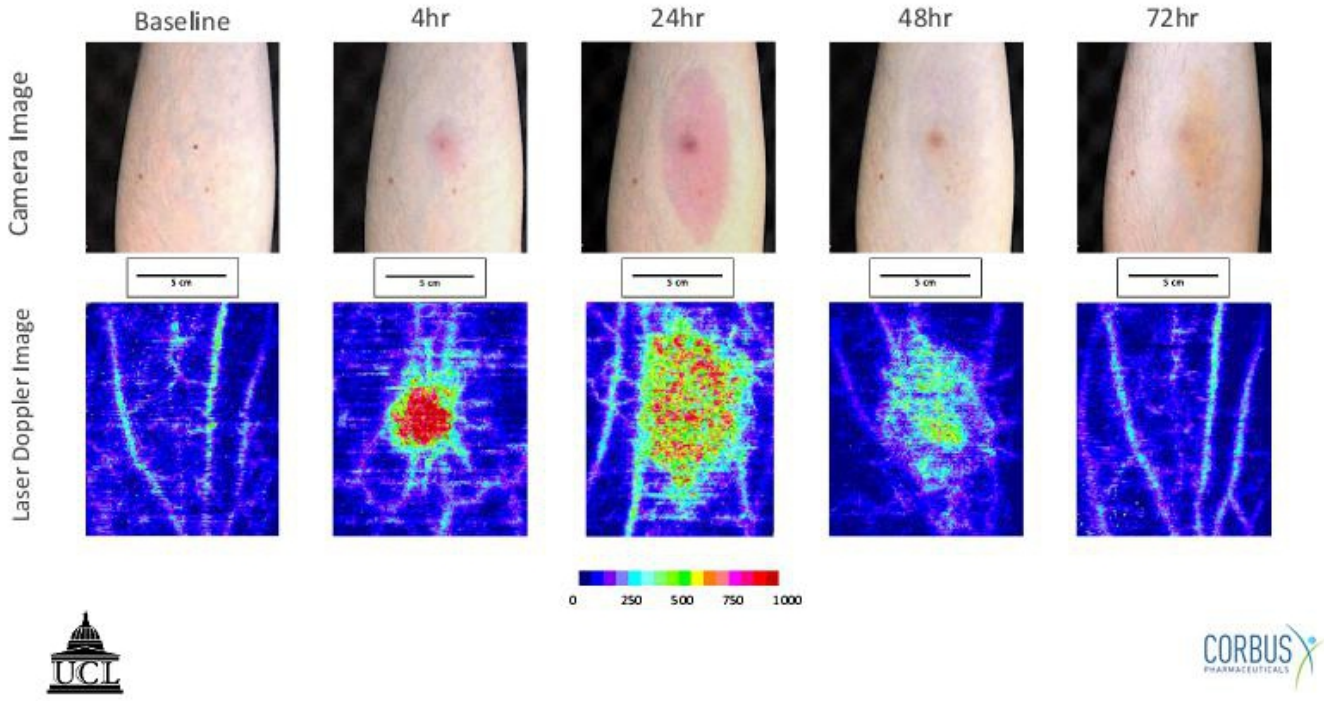
Original Article

Novel translational model of resolving inflammation triggered by UV-killed *E. coli*

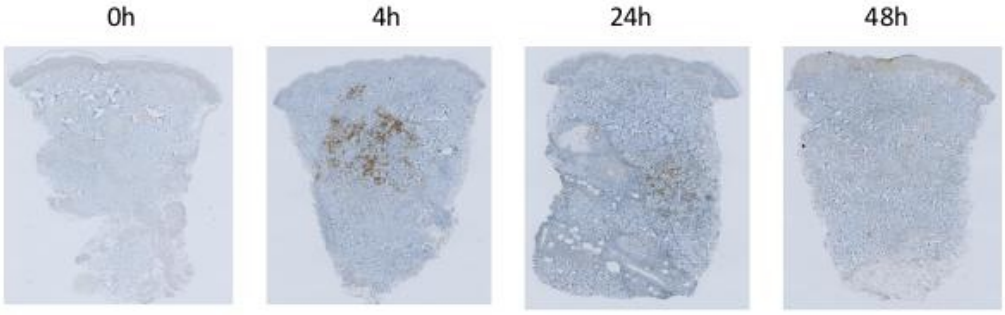
Madhur P Motwani,[1] Julia D Flint,[1] Roel PH De Maeyer,[1] James N Fullerton,[1] Andrew M Smith,[1] Daniel JB Marks[2] and Derek W Gilroy[1]*

UCL

CORBUS PHARMACEUTICALS

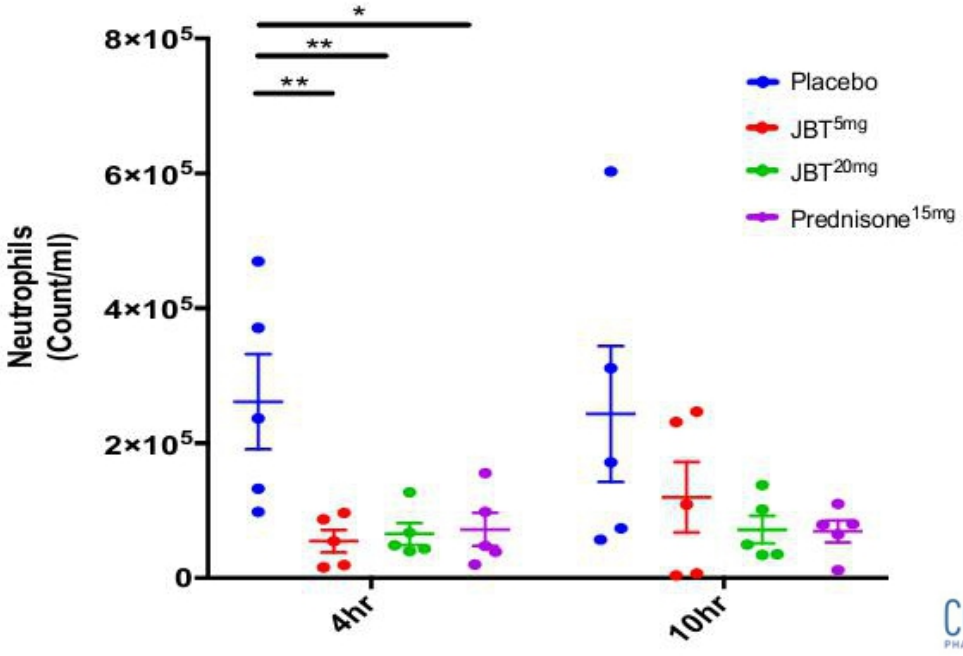

Baseline
4hr
24hr
48hr
72hr
Camera Image
Laser Doppler Image
5 cm
0
250
500
750
1000
UCL
CORBUS
PHARMACEUTICALS

ENDOTOXIN CLEARANCE

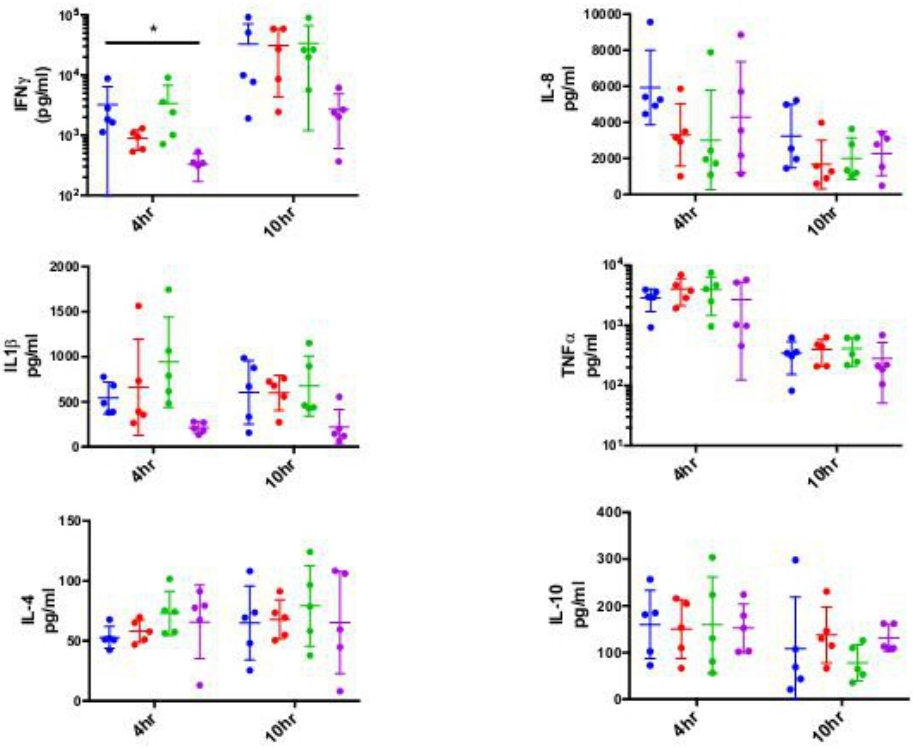



Study groups
A : Placebo, BD
B : anabasum 5mg, BD day 1-4am
C : anabasum 20mg, BD Day 1-4am
D : Prednisone 15mg, OD Day 1-4am
• Doppler • Blood • i.d. UVkEc
• Doppler • Blood • Blister
• Doppler • Blood • Blister
• Doppler • Blood
• Doppler • Blood
• Doppler • Blood
Screening
Day 1
Day 2
Day 3
Day 4 (0hr. UVkEc injection)
Day 4 (4hr after UVkEc injection)
Day 4 (10hr after UVkEc injection)
Day 5 (24hr after UVkEc injection)
Day 6 (48hr after UVkEc injection)
Day 7 (72hr after UVkEc injection)

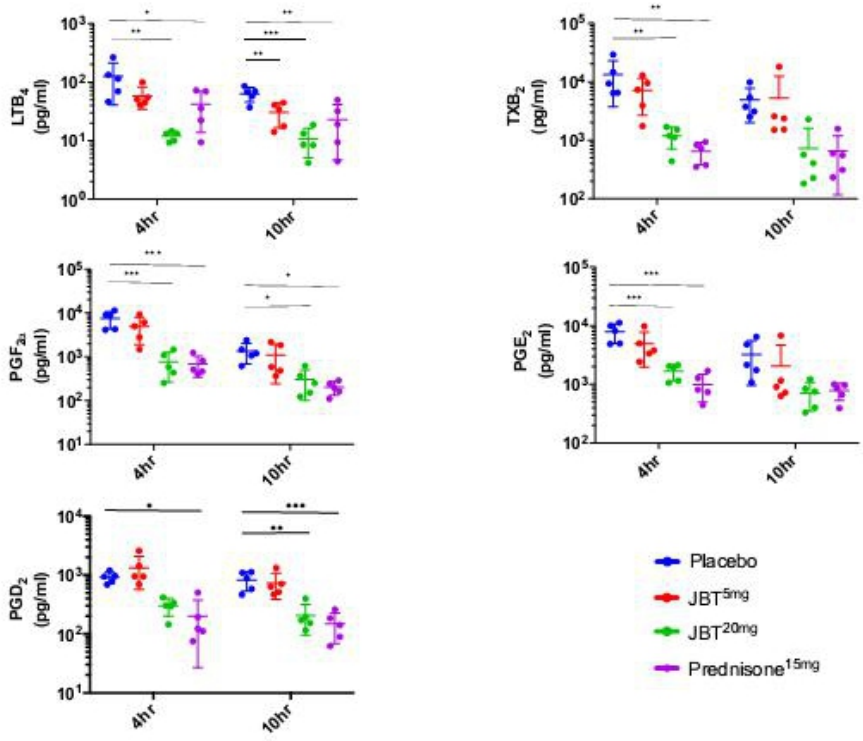
BLISTER PMNs

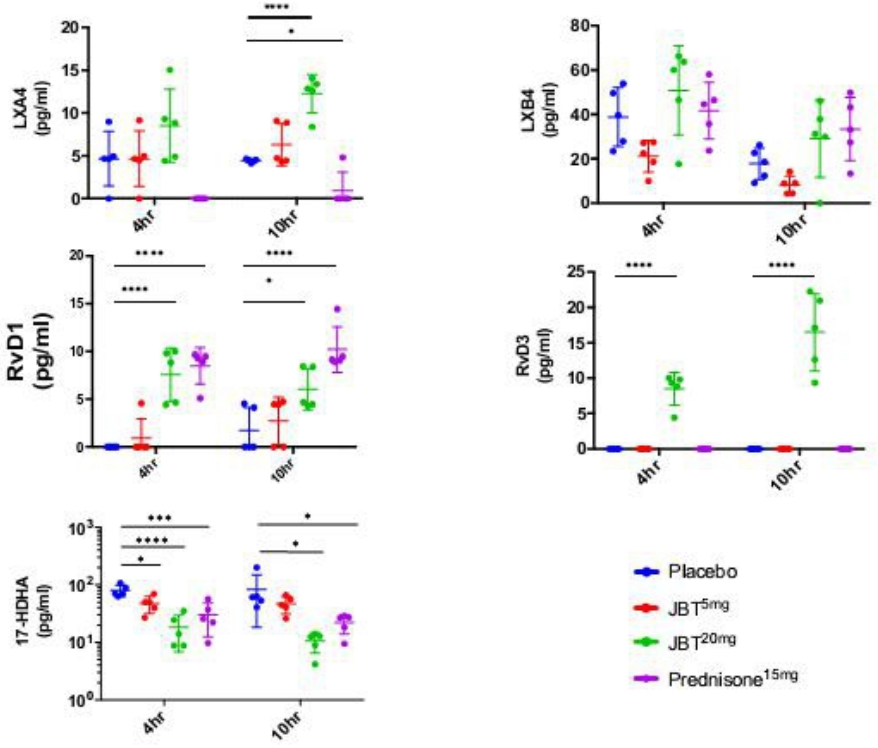


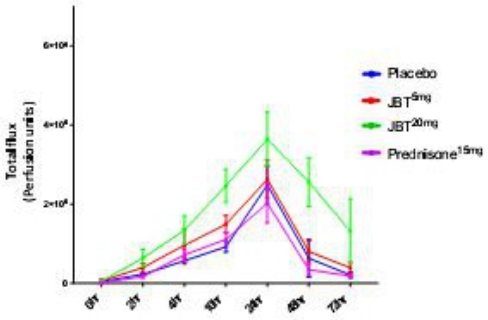
CYTOKINES/CHEMOKINES

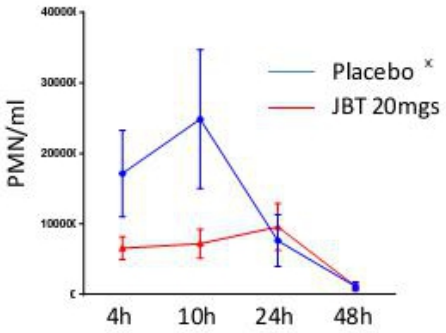

IFNγ (pg/ml)
*
4hr
10hr
IL-8 pg/ml
IL1β pg/ml
TNFα pg/ml
IL-4 pg/ml
IL-10 pg/ml

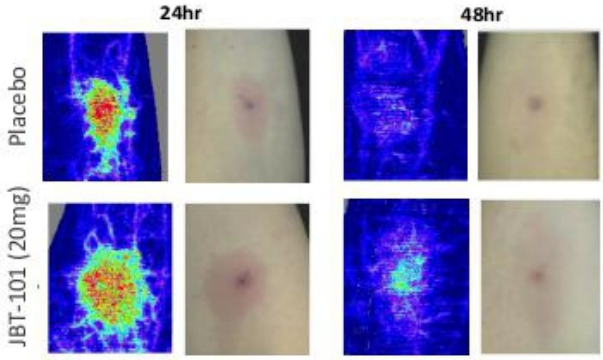
LIPIDS


LTB4 (pg/ml)
TXB2 (pg/ml)
PGF2α (pg/ml)
PGE2 (pg/ml)
PGD2 (pg/ml)
4hr
10hr
Placebo
JBT5mg
JBT20mg
Prednisone15mg


LXA4 (pg/ml)
LXB4 (pg/ml)
RvD1 (pg/ml)
RvD3 (pg/ml)
17-HDHA (pg/ml)
4hr
10hr
Placebo
JBT5mg
JBT20mg
Prednisone15mg

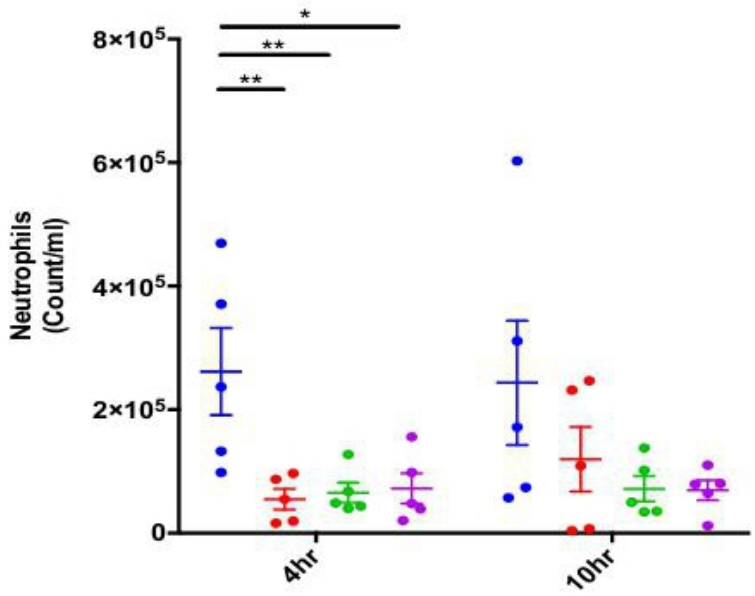

Total flux (Perfusion units)
Placebo
JBT5mg
JBT20mg
Prednisone15mg

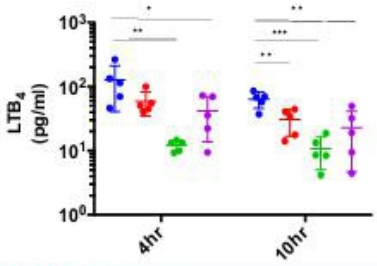

PMN/ml
Placebo
JBT 20mgs
4h
10h
24h
48h


24hr
48hr
Placebo
JBT-101 (20mg)

MECHANISM

PRIMARY ENDPOINT





CONCISE REPORT

Leukotriene B_4 is a Potent and Stereospecific Stimulator of Neutrophil Chemotaxis and Adherence

By Jan Palmblad, Curt L. Malmsten, Ann-Mari Uden, Olof Rådmark, Lars Engstedt, and Bengt Samuelsson

We studied the effects of leukotrienes on in vitro functions of neutrophil polymorphonuclear (PMN) granulocytes. Leukotriene B_4 (LTB_4) evoked a stimulated and directed migration of neutrophils under agarose with an optimum concentration of 10^{-8}M, whereas two nonenzymatically formed isomers (compounds I and II) induced this response at 10^{-7}M. Leukotriene C_4 (LTC_4) and 5-hydroxyeicosatetraenoic acid (5-HETE) did not affect this PMN migration. At the same optimum concentrations, LTB_4 and compounds I and II augmented PMN adherence to nylon fibers. The chemotactic and adherence responses were of the same magnitude as with formyl-Met-Leu-Phe (fMLP) at 10^{-8}M. None of the leukotrienes influenced the spontaneous or phagocytosis-associated chemiluminescence or the ability to kill *Staphylococcus aureus*. The cyclooxygenase inhibitor, indomethacin, inhibited only partly the fMLP-induced migration at high concentrations and stimulated migration at 2.5×10^{-7}M, suggesting that arachidonic acid was then mainly metabolized by the lipoxygenase pathways. The lipoxygenase and cyclooxygenase inhibitor, eicosatetraynoic acid, inhibited both spontaneous and stimulated migration at $\geq 2.5 \times 10^{-7}$M, but not at lower concentrations. Thus, since LTB_4, and to a lesser degree compounds I and II, stimulated migration and adhesion, it is suggested that these mediators could be of importance for the emigration of neutrophils from blood vessels to areas of inflammation.

ANNALS of THE NEW YORK ACADEMY OF SCIENCES

ARACHIDONIC ACID, LEUKOTRIENE B_4, AND NEUTROPHIL ACTIVATION*

P. H. Naccache and R. I. Sha

Departments of Pathology and Phys
University of Connecticut Health C
Farmington, Connecticut 060

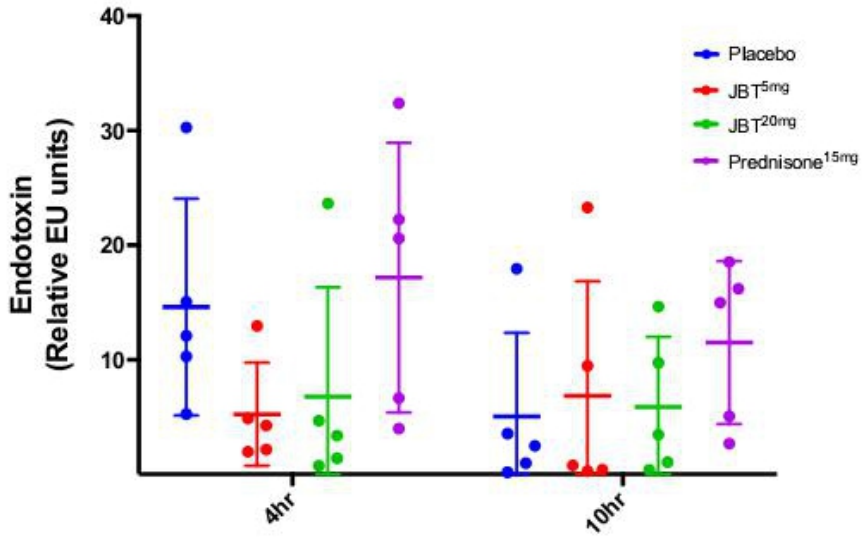
Immunology 1983 **50** 35

Enhancement of human neutrophil adherence by synthetic leukotriene constituents of the slow-reacting substance of anaphylaxis

E. J. GOETZL, L. L. BRINDLEY & D. W. GOLDMAN *Howard Hughes Medical Institute Laboratories and Department of Medicine, University of California, San Francisco, California, U.S.A.*

Accepted for publication 14 March 1983

ENDOTOXIN CLEARANCE

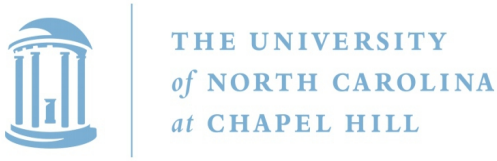


Q&A

CF: Biochemistry of Inflammation and *Ex-Vivo* Lung Macrophage Data

Michael Knowles, M.D.

Professor of Pulmonary and Critical Care Medicine at University of North Carolina Chapel Hill and member of the Company's Scientific Advisory Board, and expert in inflammation in CF



INFLAMMATION IN CYSTIC FIBROSIS (CF) LUNG DISEASE

- Lung disease in CF is initiated by thick mucus, reflecting mutant CFTR and failure to fully hydrate bronchial mucus, which results in defective mucociliary clearance
- Infection occurs rapidly due to defective mucociliary clearance, and the associated inflammatory response to infection is severe and persistent
- Infection and inflammation includes a massive influx of neutrophils, which contributes to irreversible damage to bronchi ("bronchiectasis")
- Anti-inflammatory therapy (systemic steroids, 1980s; high-dose ibuprofen,1990s) slow/reduce bronchial wall damage and loss of lung function, but are not currently used due to adverse effects
- Pulmonary macrophages are critical innate host defense cells in the lung, as ingest & kill microbes and secrete inflammatory mediators in response to infection
- Pulmonary macrophages from CF patients exhibit exaggerated basal and LPS-induced cytokine (TNF-α & IL-6) production*, which contributes to irreversible lung damage

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*Lubaba, B.....Ribiero, C., 2015, Am J Respir Crit Care Med

CORBUS PHARMACEUTICALS

EFFECT OF ANABASUM (CB2 RECEPTOR AGONIST) ON CYTOKINE PRODUCTION BY PULMONARY MACROPHAGES FROM CF PATIENTS

Rationale: Macrophages play a key role in lung host defense, and secrete inflammatory mediators in response to microbial infection. Pulmonary macrophages from CF patients are hyper-inflammatory*, and contribute to progressive and irreversible lung damage.

Objective: To determine the effect of anabasum on production and secretion of inflammatory cytokines by CF pulmonary macrophages

Study Design: Isolated macrophages from lungs excised from two CF patients undergoing lung transplant.*

- Cultured and treated macrophages with Pseudomonas LPS (100 ng/ml) to stimulate a cytokine (inflammatory) response
- Treated macrophages with anabasum (1, 3, 10 **µ**M) after LPS ("4 hrs"), at same time as LPS ("6 hrs"), and for 24 hrs before LPS ("24 hrs")
- Collected supernatant at 6 hrs post-LPS and tested by Elisa for TNF-α, IL-6, and other cytokines

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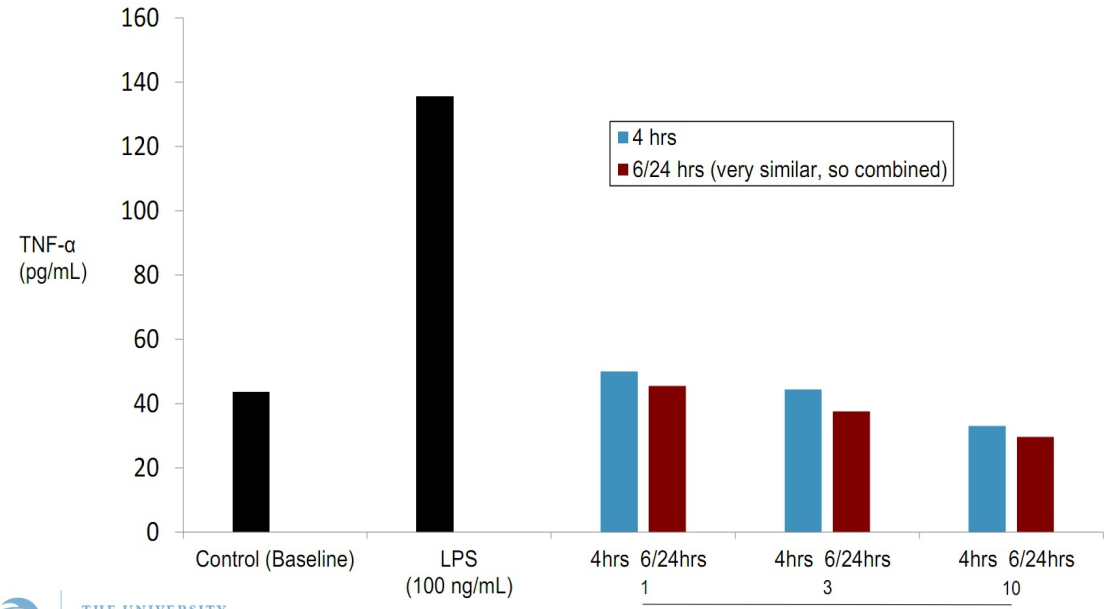
*Lubaba, B.…….Ribiero, C., 2015, Am J Respir Crit Care Med

CORBUS PHARMACEUTICALS

EFFECT OF ANABASUM ON TNF-α PRODUCTION BY LPS-TREATED CF PULMONARY MACROPHAGES*

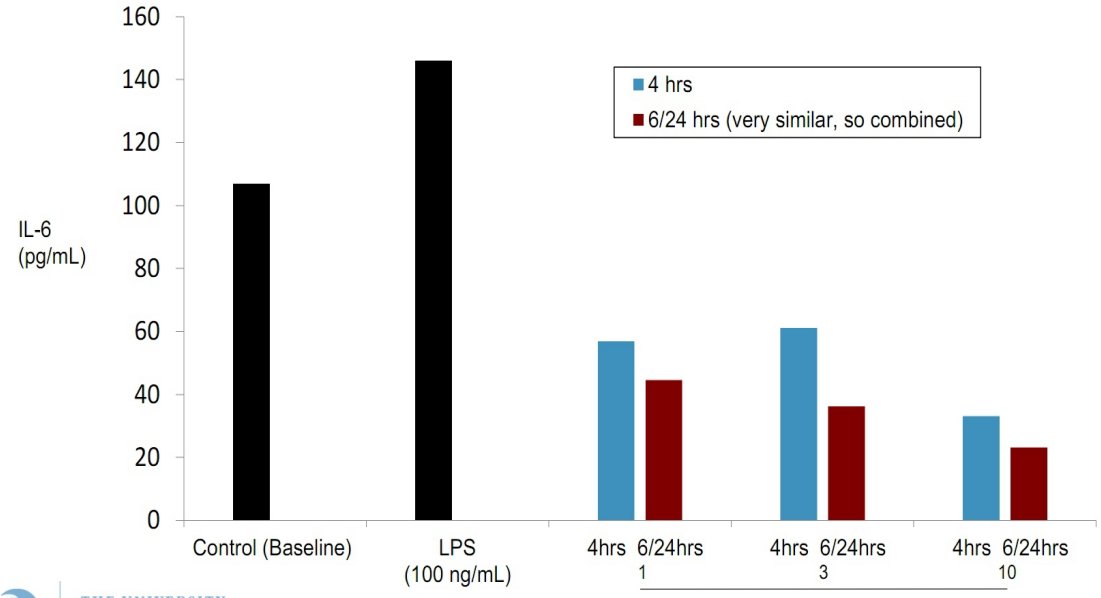


THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

*Mean data on macrophages from two CF patients

CORBUS PHARMACEUTICALS

EFFECT OF ANABASUM ON IL-6 PRODUCTION BY LPS-TREATED CF PULMONARY MACROPHAGES*



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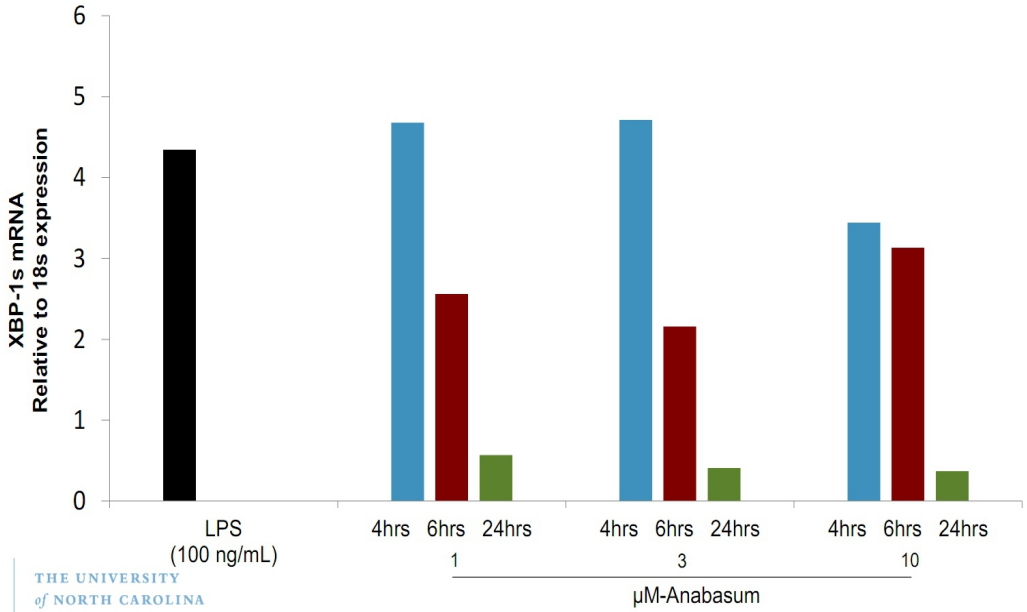
*Mean data on macrophages from two CF patients

CORBUS PHARMACEUTICALS

EFFECT OF CB2 RECEPTOR AGONIST (ANABASUM) ON EXPRESSION OF XBP-1s IN CF PULMONARY MACROPHAGES*: A MARKER OF INFLAMMATORY RESPONSE**



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CORBUS PHARMACEUTICALS

*Mean data on macrophages from two CF patients; **Lubamba, B……Ribiero, C., 2015, Am J Respir Crit Care Med

CONCLUSIONS

- Anabasum inhibited LPS stimulated production of TNF-α and IL-6 by CF pulmonary macrophages in a dose-dependent fashion (up to >75% inhibition)
- Anabasum inhibited LPS stimulated production of TNF-α and IL-6 by CF pulmonary macrophages, whether anabasum was dosed before LPS, at same time, or after LPS.
- Anabasum inhibited expression in CF pulmonary macrophages of XBP-1s, which has a role in LPS-induced ER stress and inflammatory response*.
- Taken together, these results indicate that anabasum has the potential to modify macrophage-mediated inflammation in the lungs of CF patients, and offers a novel approach to benefit all CF patients, regardless of genotype.

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*Lubaba, B.....Ribiero, C., 2015, Am J Respir Crit Care Med

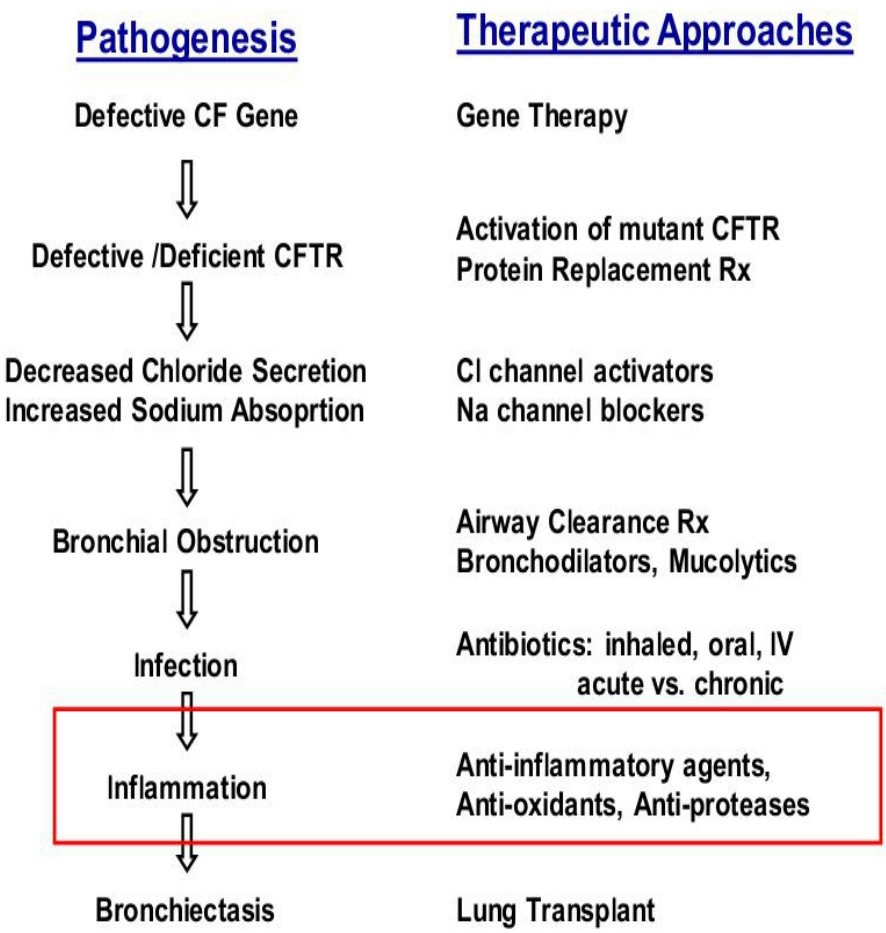
CORBUS PHARMACEUTICALS

Q&A

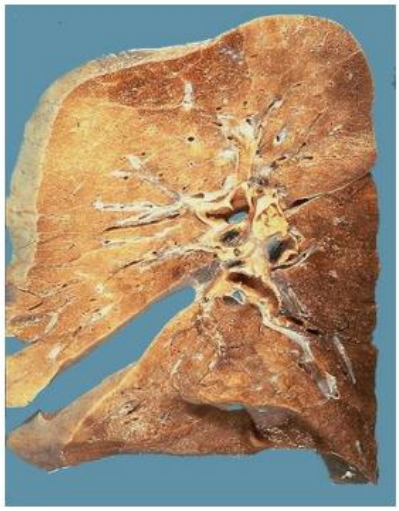
CF Phase 2 Study: Role of Inflammation, Protocol, Study Design and Outlook

James Chmiel, M.D., M.P.H.

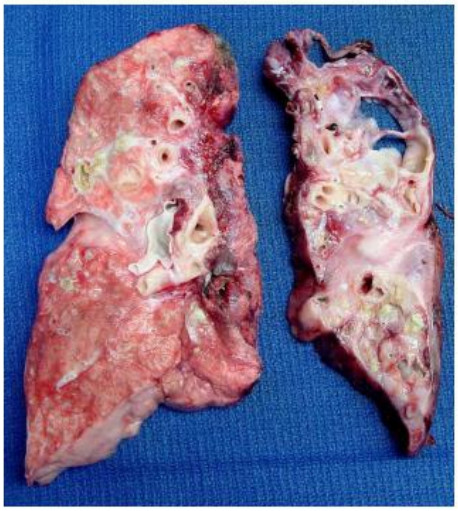
Professor of Pediatrics, Case Western Reserve University, Associate Director of the LeRoy W. Matthews Cystic Fibrosis Center at University Hospitals Rainbow Babies and Children's Hospital in Cleveland, and Principle Investigator of the Company's Phase 2 cystic fibrosis clinical study


Pathogenesis
Therapeutic Approaches
Defective CF Gene
Gene Therapy
Defective /Deficient CFTR
Activation of mutant CFTR
Protein Replacement Rx
Decreased Chloride Secretion
Increased Sodium Absoprtion
Cl channel activators
Na channel blockers
Bronchial Obstruction
Airway Clearance Rx
Bronchodilators, Mucolytics
Infection
Antibiotics: inhaled, oral, IV
acute vs. chronic
Inflammation
Anti-inflammatory agents,
Anti-oxidants, Anti-proteases
Bronchiectasis
Lung Transplant

Normal

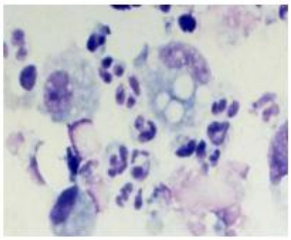


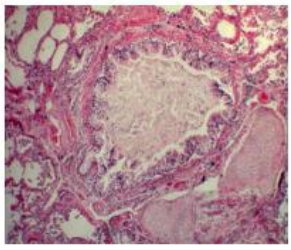
Cystic Fibrosis



Inflammation in the CF Lung Disease

- **Begins early in life**
- **Directly linked to the basic defect**
  - May be present in the absence of infection
- **Excessive relative to the burden of bacteria**
- **Neutrophils and their products are key offenders**
  - Persistent influx of neutrophils
  - Release proteases, oxidants, DNA, chemoattractants (IL-8, LTB_4)
- **Plays a key role in lung damage**





Konstan and Saiman
NACFC 2009; Plenary Session II

CORBUS PHARMACEUTICALS

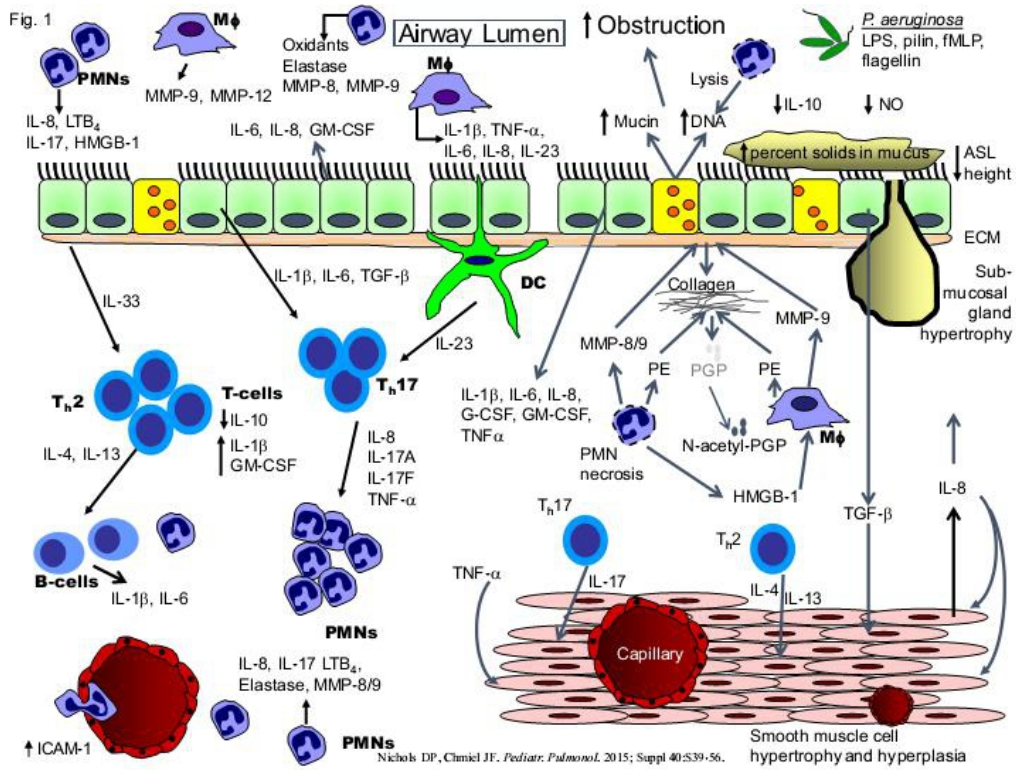


Fig. 1
PMNs
IL-8, LTB4
IL-17, HMGB-1
MΦ
MMP-9, MMP-12
Oxidants
Elastase
MMP-8, MMP-9
Airway Lumen
Obstruction
P. aeruginosa
LPS, pilin, fMLP,
flagellin
Lysis
Mucin
DNA
IL-10
NO
IL-6, IL-8, GM-CSF
IL-1β, TNF-α,
IL-6, IL-8, IL-23
percent solids in mucus
ASL
height
ECM
Sub-
mucosal
gland
hypertrophy
IL-1β, IL-6, TGF-β
DC
IL-33
IL-23
Collagen
MMP-9
MMP-8/9
PE
PGP
PE
Th2
T-cells
IL-10
IL-1β
GM-CSF
Th17
IL-4, IL-13
IL-8
IL-17A
IL-17F
TNF-α
IL-1β, IL-6, IL-8,
G-CSF, GM-CSF,
TNFα
PMN
necrosis
N-acetyl-PGP
MΦ
HMGB-1
IL-8
TGF-β
Th17
Th2
B-cells
IL-1β, IL-6
PMNs
TNF-α
IL-17
IL-4
IL-13
Capillary
IL-8, IL-17 LTB4,
Elastase, MMP-8/9
ICAM-1
PMNs
Smooth muscle cell
hypertrophy and hyperplasia
Nichols DP, Chmiel JF. Pediatr. Pulmonol. 2015; Suppl 40:S39-56.

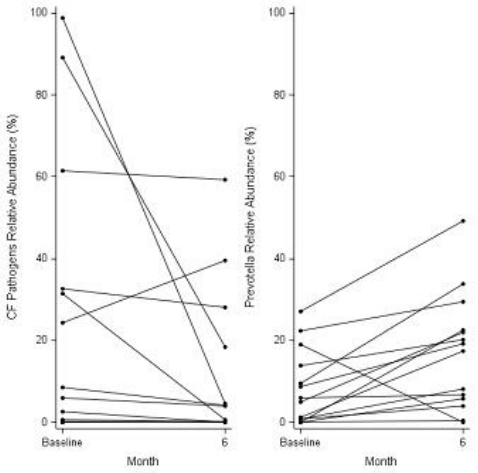
Anti-Inflammatory Trials in CF

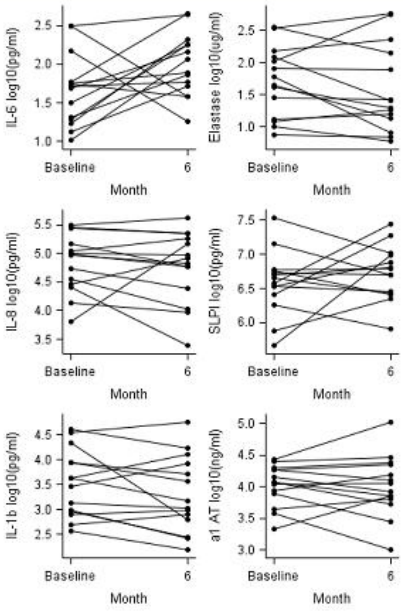
Anti-inflammatory Approaches

- Broad-based (multi-specific) agents
  - Azithromycin, Corticosteroids, ibuprofen & other NSAIDs, JBT-101, airway clearance, mucolytics, mucus hydrators
- Specific drugs and biologic agents
  - KB001A (*P. aeruginosa* TTSS), GMI-1051 (*P. aeruginosa* PA-IL, PA-IIL), Cytokine/eicosanoid inhibitors/antagonists, NF-$_{\kappa}$B and p38 MAPK inhibitors, IL-10, PPAR agonists, statins, PDE_4 inhibitors, LTB_4 receptor antagonists, adhesion molecule inhibitors, Dornase alfa (DNA), α1-antitrypsin (elastase), antioxidants, others

CORBUS PHARMACEUTICALS

Are Anti-inflammatory Drugs Still Necessary?
Impact of Ivacaftor on Pulmonary Inflammation in G551D

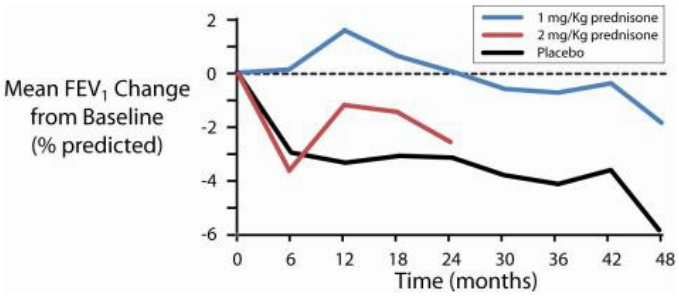




Rowe SM, et al. Am J Respir Crit Care Med. 2014;190:175-184

Proof of Concept: Oral Corticosteroids

Alternate-day prednisone trials demonstrated the benefits of anti-inflammatory therapy

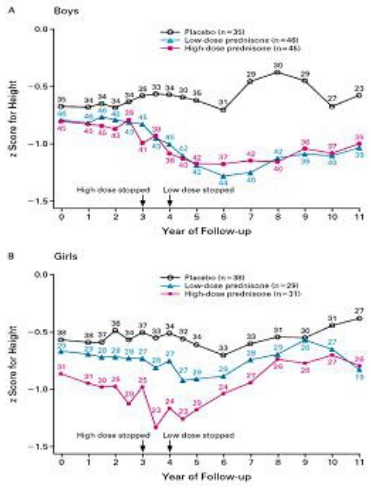


Eigen H et al. J Pediatr 1995

Long-Term Follow-Up 4-yr Prednisone Trial

Growth and PFT assessed 6-7 years after completion of trial

- Growth impairment persisted, particularly in boys
- Pulmonary function benefit not sustained



Lai et al. NEJM 342:851, 2000

Growth following prednisone therapy

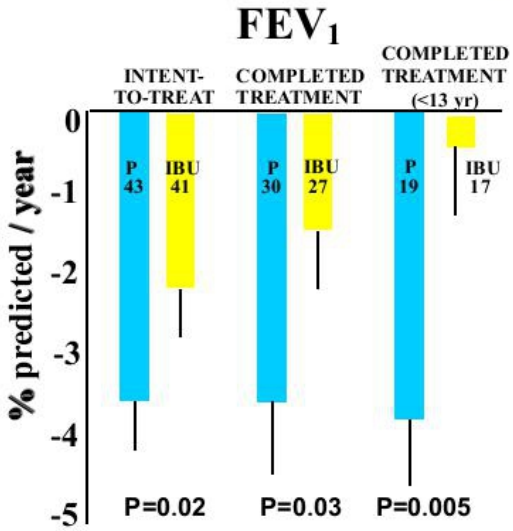
Clinical Trial of High-Dose Ibuprofen

STUDY DESIGN:

- 4 year DB/PC
- 85 CF pts, age 5-39 yrs
- Mild lung disease
  (FEV1 > 60% pred)
- Ibu 20-30 mg/kg BID

RESULTS:

- Slowed PFT decline
- Slowed CXR deterioration
- Preserved IBW
- Reduced hospitalizations
- Reduced con. meds



Konstan et al. NEJM 332:848, 1995

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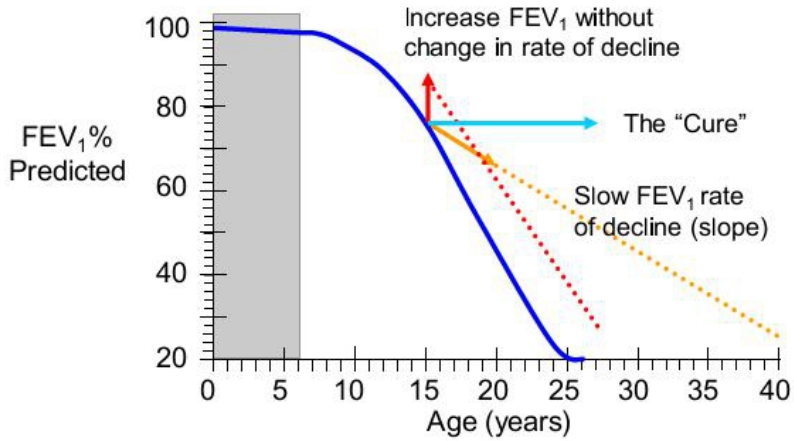
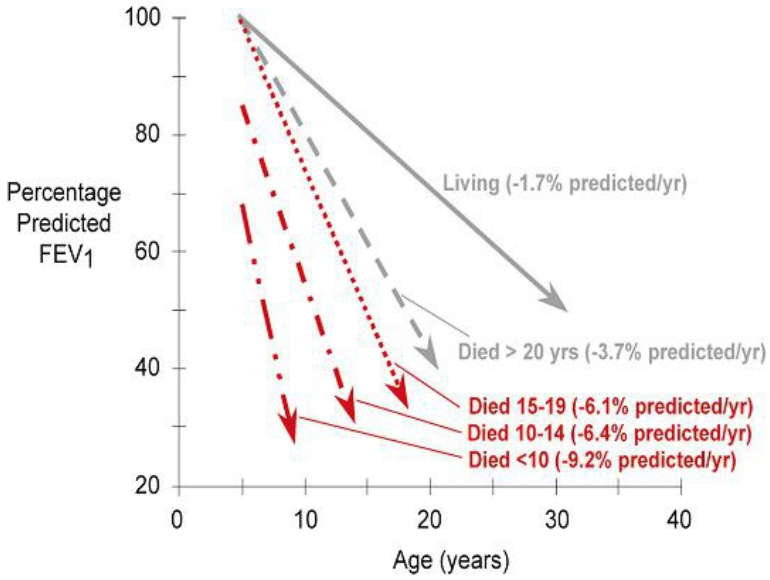
Extrapolating Relative Benefit

Improvement in FEV_1 vs. Slowing the Rate of Decline



Corey et al., J Pediatr 1997; 131:809-814
Schluchter et al., Statistics in Medicine 2002; 21:1271-1287

Linking FEV_1 to Survival



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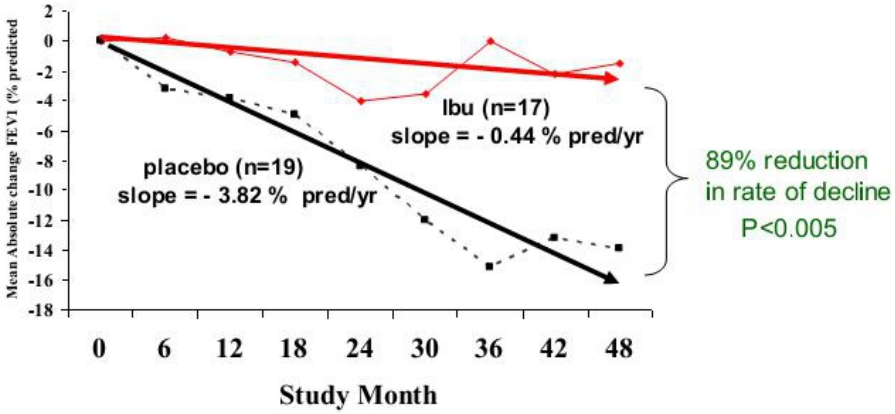
Annualized Rate of Decline of FEV_1 % pred

Ibuprofen Clinical Trial

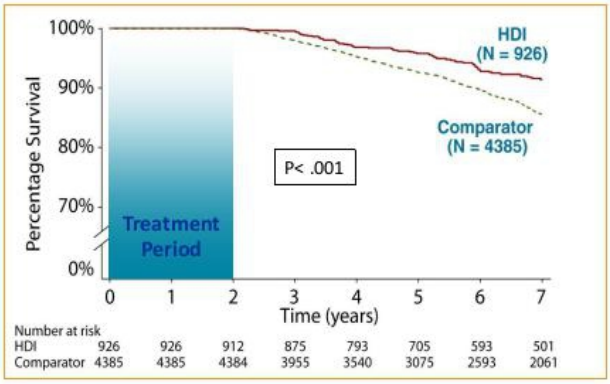
5 to 13 yr (efficacy)



Konstan et al. NEJM 1995

ESCF Registry:
Ibuprofen Therapy Improves Survival

Unadjusted Time to All-Causes Mortality



Kaplan-Meier:

- **HDI survival = 91.5% [89.5%, 93.5%]**
- **Comparator = 85.6% [84.4%, 86.8%]**

Unadjusted Cox proportional hazard = 0.522 (P<.001)

Adjusted* Cox proportional hazard = 0.736 (P=.025)

*17 covariates derived from regression of propensity variables

VanDevanter et al. NACFC 2012

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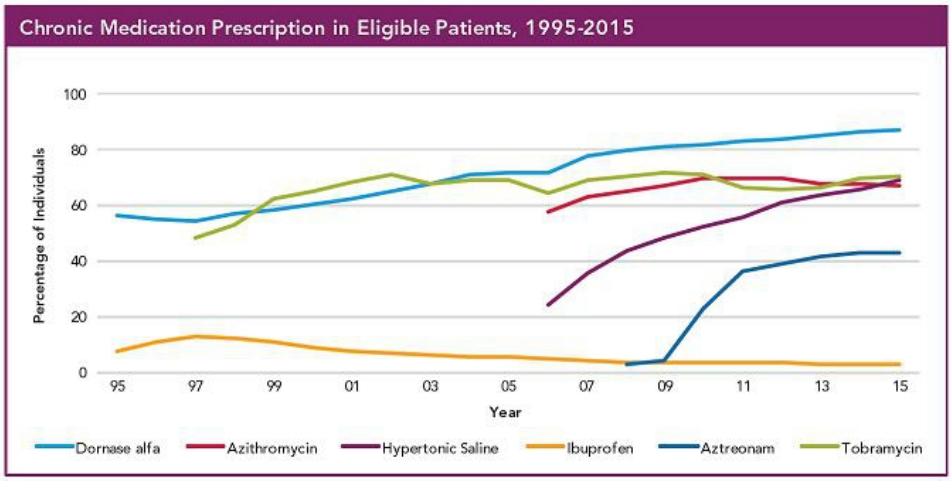
Potential Barriers to Ibuprofen Use in CF

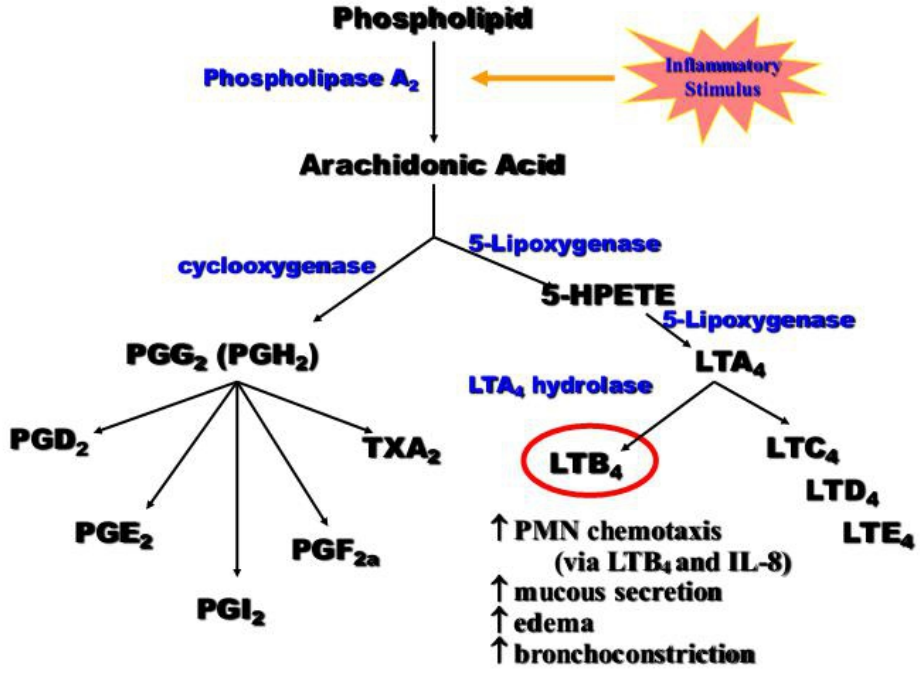
- Beneficial effect on lung disease not accepted
- Concerns regarding safety
- Establishing individualized dose through pharmacokinetic testing logistically difficult

Ibuprofen therapy not adopted by the CF Community



2015 Median Use: 0.0 % of 6-12 yo with FEV1 > 60 % pred

CFF Patient Registry 2015 Annual Data Report, October 2016


Phospholipid
Phospholipase A2
Inflammatory Stimulus
Arachidonic Acid
cyclooxygenase
5-Lipoxygenase
5-HPETE
5-Lipoxygenase
PGG2 (PGH2)
LTA4
LTA4 hydrolase
PGD2
TXA2
LTB4
LTC4
LTD4
LTE4
PGE2
PGF2a
PGI2
↑ PMN chemotaxis
(via LTB4 and IL-8)
↑ mucous secretion
↑ edema
↑ bronchoconstriction

Immune Over-suppression?

- BIIL 284 BS
  - LTB_4 receptor antagonist
  - Suppresses neutrophil invasion
- Phase 1 study: single dose (N=30) and 14 day multi-dose (N=24) safety/PK study
- Multinational Phase 2 study
  - 6 months, 600 CF patients
  - Halted early (after 420 pts) due to safety concerns
    - Increased risk of pulmonary exacerbation

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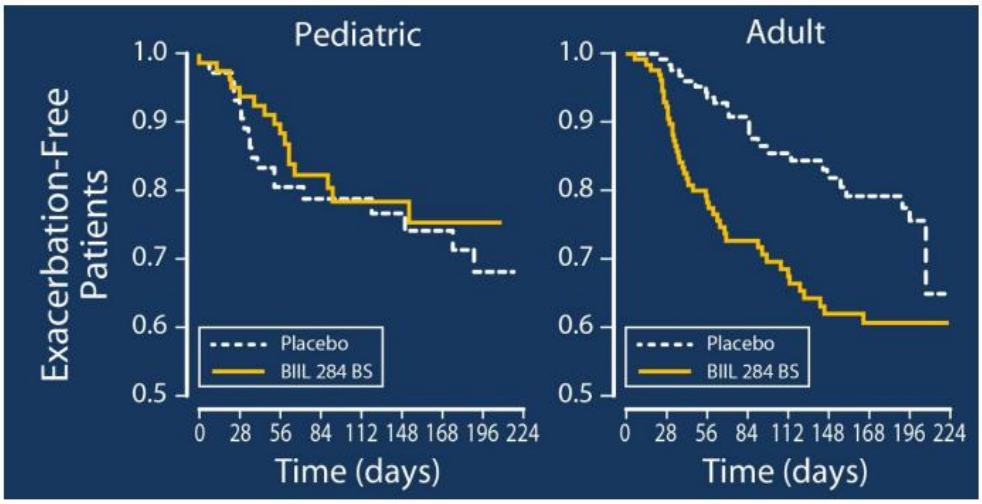
BIIL 284 Phase 2 Time to Exacerbation



Konstan et al. J Cystic Fibros 2014;13:148–155

Was BIIL 284 too Suppressive?

- Hypothesis that over-suppression of neutrophil invasion may have led to changes in microbial community
  - Resulting in increased respiratory signs and symptoms in patients
- BIIL 284 mouse study*
  - Mouse airways infected with *P. aeruginosa*
  - Mice treated with varying doses of BIIL 284
  - Neutrophil counts *and P. aeruginosa* CFU measured in airway lavage fluids

* Döring et al. J Cystic Fibros 2014;13:156–163

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CF Inflammation: A Nuanced Target

- An exaggerated immune response has long term negative consequences for the CF lung

HOWEVER…

- The immune system also plays a critically *positive* role in the CF lung
  - Despite extremely high bacterial burdens in the lung lumen, CF patients *rarely* develop bacteremia
- Unlike bacteria or sticky mucus or apical surface dehydration, *elimination* of the CF immune system is not a desirable therapeutic goal

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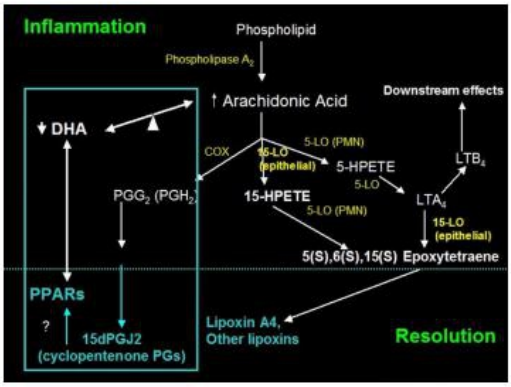
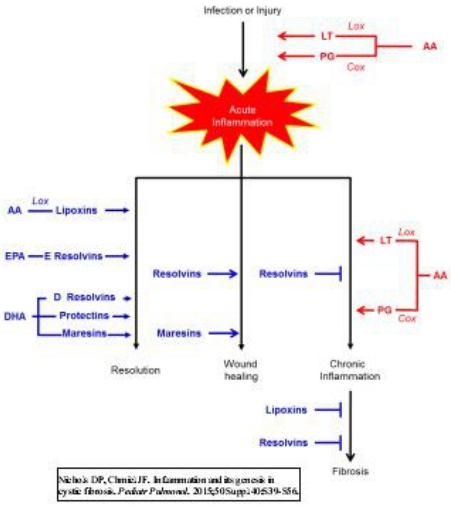
Speculation

Rather than trying to turn off pro-inflammatory pathways with therapeutics, perhaps the more prudent approach is to upregulate the body's own counter-regulatory mechanisms

Arachidonic Acid Pathway involved in Pathways that both promote and Resolve Inflammation

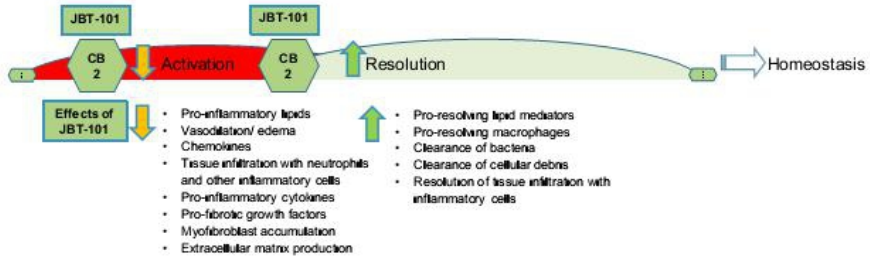




Nichols DP, Clancy JF. Inflammation and its genesis in cystic fibrosis. *Pediatr Pulmonol*. 2015;50 Suppl 40:S39-S56.

JBT-101 SHIFTS THE BALANCE FROM ACTIVATION TO RESOLUTION OF INNATE IMMUNE AND FIBROTIC RESPONSES

Impact of JBT-101 on the course of a persistent innate immune response



JBT-101 is not immunosuppressive

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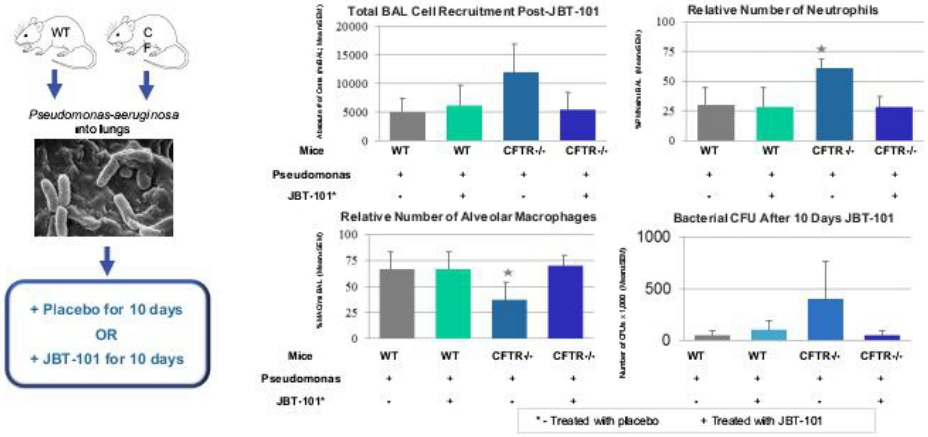
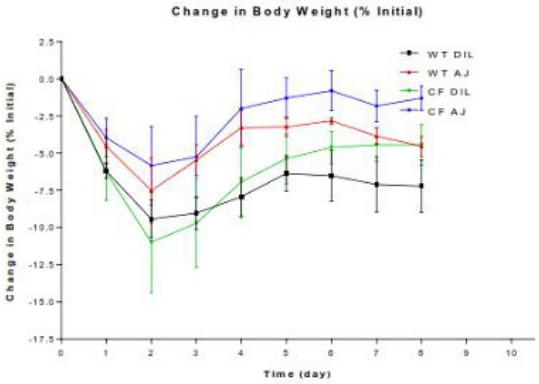
JBT-101 REDUCES CHRONIC INFLAMMATION AND RESOLVES PERSISTENT INFECTION IN A MOUSE MODEL OF CYSTIC FIBROSIS



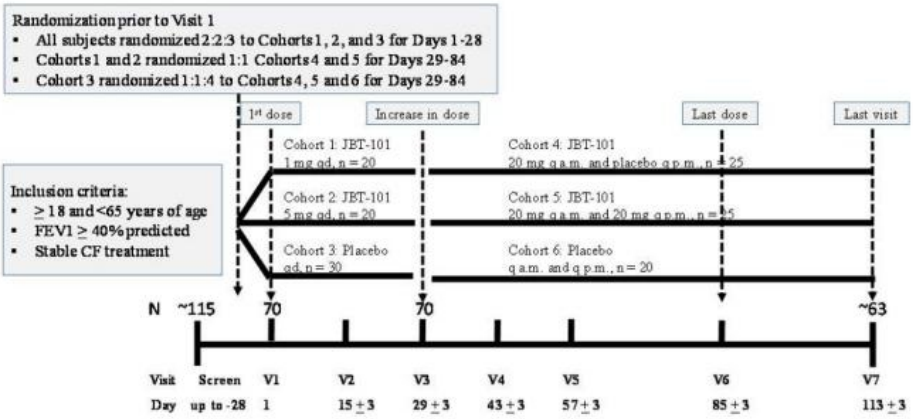
JBT-101 REDUCES WEIGHT LOSS AND IMPROVES SURVIVAL IN A MOUSE MODEL OF CYSTIC FIBROSIS



GROUP	SURVIVAL RATE DAY 10
WT	5/5 (100%)
WT + JBT-101	5/5 (100%)
CF	3/5 (60%)
CF + JBT-101	5/5 (100%)

Bonfield, Tracey; Tepper, Mark 2015

Study Design



JBT-101: CF PHASE 2 CLINICAL STUDY

Top-Line Data Expected 1Q17

Primary Endpoint:
Safety and Tolerability

Secondary Endpoints:
Metabolipidomic profile
Trends in FEV1, CFQ-R

Study Completed:
Last subject last visit 28 Dec 2016

- Double-blind, randomized, placebo-controlled study in the U.S. and EU
- **Primary endpoints:** Safety/ tolerability
- **Secondary endpoints:** Metabolipidomic profile for MOA, trends in efficacy (FEV1, Lung Clearance Index, CFQ-R Respiratory Symptom Score)
- **Exploratory endpoints:** Biomarkers of disease activity and inflammation in blood and sputum, microbiota in the lungs, PK
- **Patient number:** 85 adults with CF at 21 sites US, UK, Germany, Italy, and Poland
- **Treatment duration:** 84 days treatment with 28 days follow-up
- **Dose response:** 1 mg/day, 5 mg/day, 20 mg/day and 20 mg/day twice a day

	Q2 2015	Q3 2015	Q4 2015	Q1 2016	Q2 2016	Q3 2016	Q4 2016	Q1 2017
IND open with FDA	✓							
Study launch		✓						
First subject dosed			✓					
Enrollment complete						✓		
Last subject last visit							✓	
Anticipated top-line study data								

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Q&A

CLOSING REMARKS

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