FUSONEX

Antibody Therapy to Treat Rare Genetic Disease
Familial Adenomatous Polyposis and Cancer

COLUMBIA | COLUMBIA UNIVERSITY IRVING MEDICAL CENTER

Yiping Han, PhD
Founder, Professor and Chief Scientist

Background

In 2012 new reports linked common oral anaerobe Fn to CRC

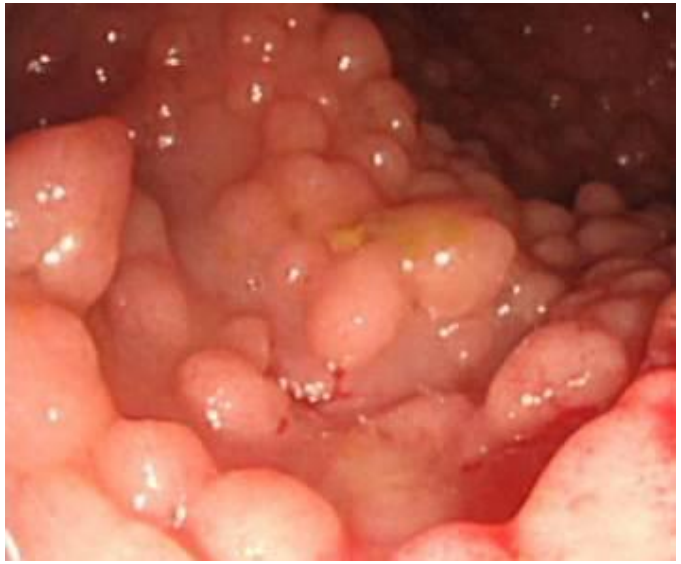
- Colorectal Cancer is the 2nd leading cause of cancer death in both men and women in the U.S.
- Lifetime risk for developing CRC is about 1 in 24
- Over the past few decades, there has **been rising CRC incidence among younger adults**
- Even as screening and treatment improves, CRC related deaths among young adults are still increasing annually

Fn contributes to CRC development by stimulating cancer cell proliferation

- *Fn* affects tumor microenvironment, causes chemoresistance, metastasis, and worsens prognosis
- *Fn* secretes amyloid-like adhesin FadA to directly promote neoplastic **progression via activation of Annexin A1** and Wnt/b-catenin signaling

Familial adenomatous polyposis (FAP)

- Hereditary disease caused by mutations in the **APC** gene
- Considered an orphan disease
- Affects 50k families in US, 60k in EU, and 140k in China
- Characterized be development of hundreds to thousands of adenomas in the rectum and colon
- If left untreated, **100% of FAP patients will develop CRC by the age of 45**
- No effective therapy other than colectomy
- Significant value for patients to delay surgery at young age

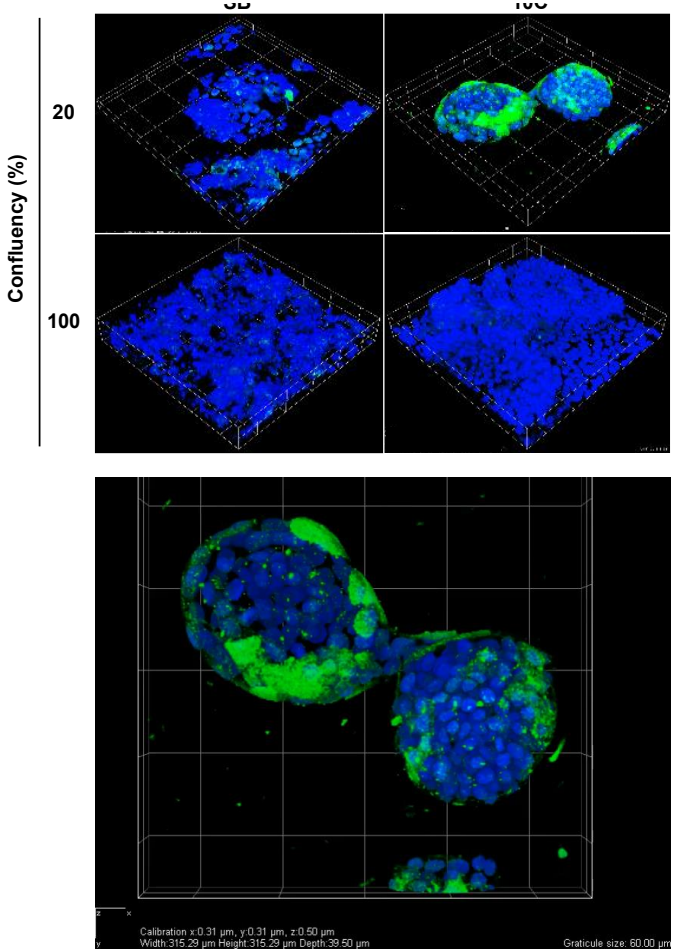


Innovation: Annexin A1

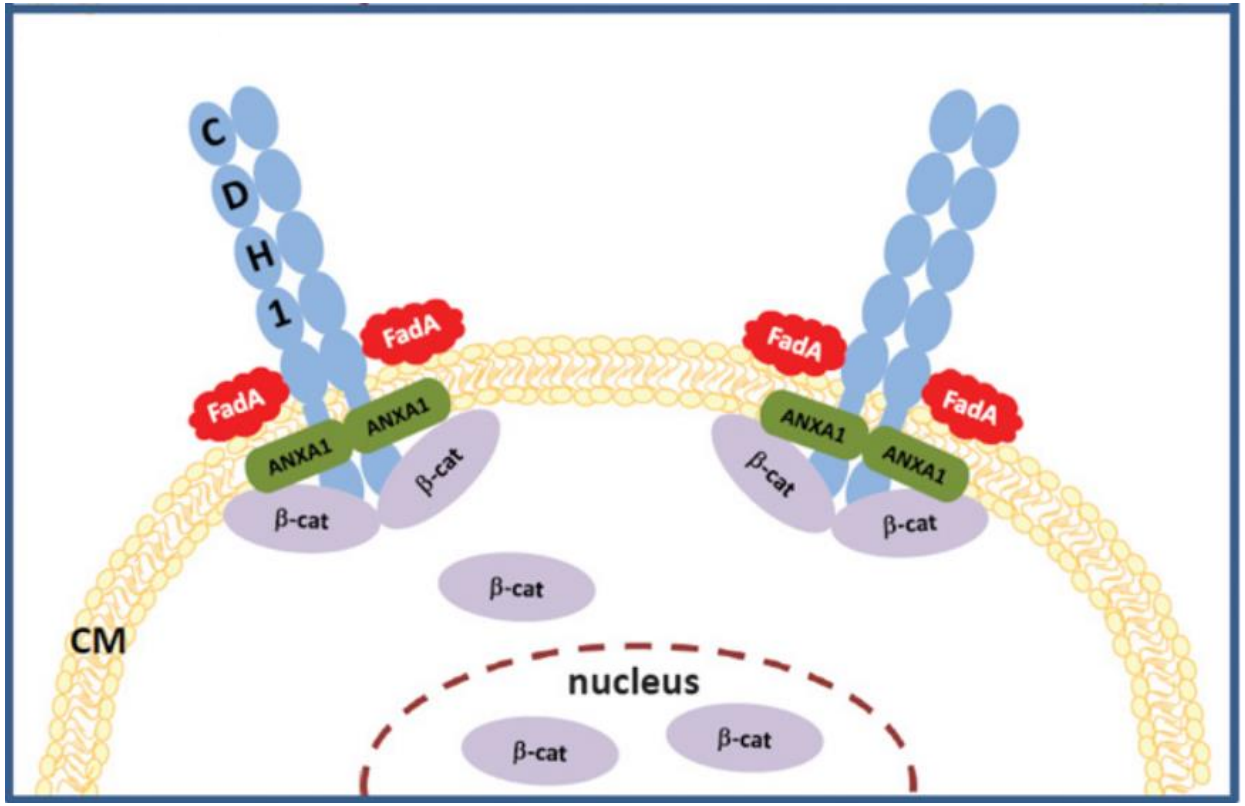
Annexin A1

- Specifically expressed on proliferating CRC cells
- Activates b-catenin signaling in CRC
- Predicts poor prognosis
- Increased in other cancers–treatment applicable to other cancers
- Global deletion in mice had no overt deleterious effects

Approach: Primary mAb



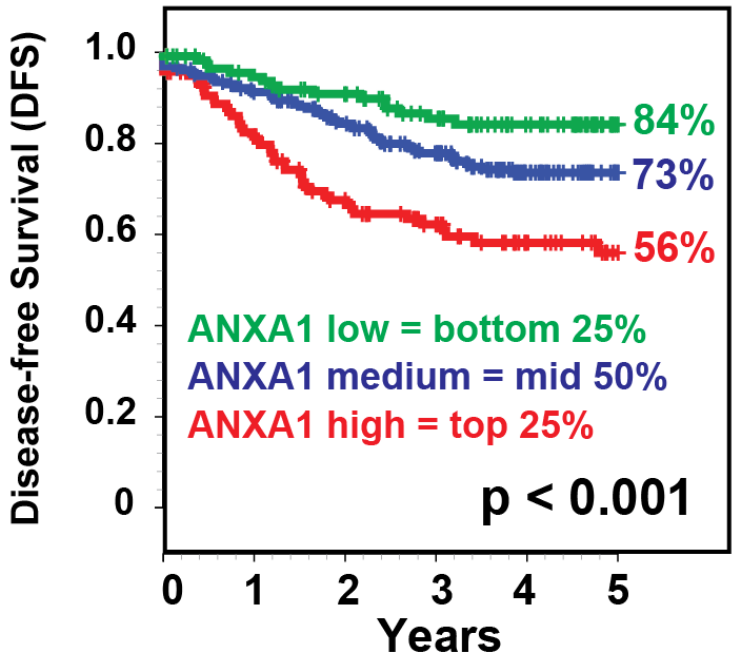
Rubinstein, M.R…… Han, Y.W., EMBO Reports 2019



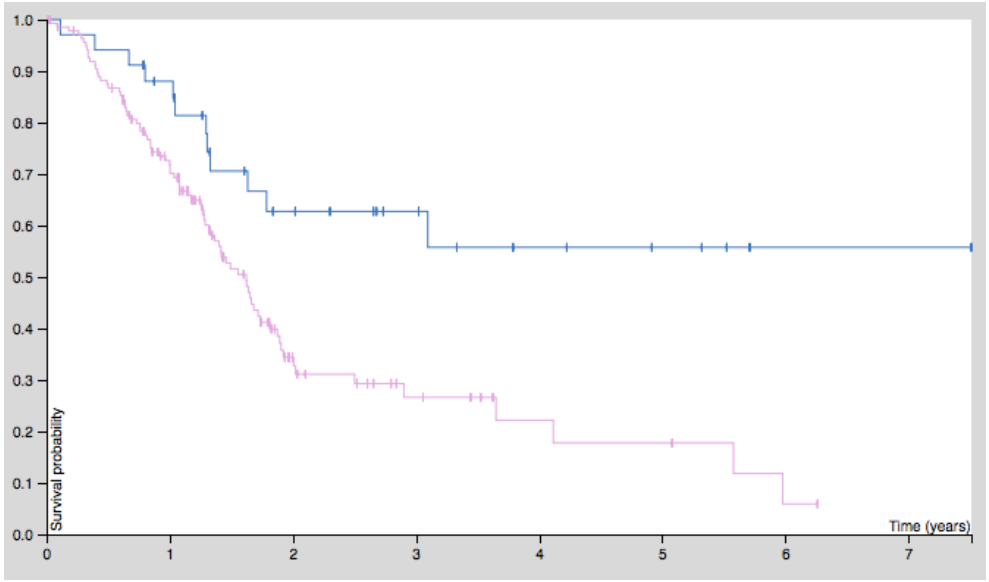
- *Fn* colonizes in CRC predominantly via GI translocation
- Amyloid FadA is a key virulence factor mediating acid tolerance, biofilm formation, binding to CRC cells and stimulating CRC growth
- FadA binds E-cadherin and activates β-catenin signaling via Annexin A1
- Annexin A1 is a previously unrecognized β-catenin modulator playing a critical role in intestinal neoplastic progression
- FadA and Annexin A1 interact via a positive feedback loop

ANXA1 predicts poor prognosis

CRC



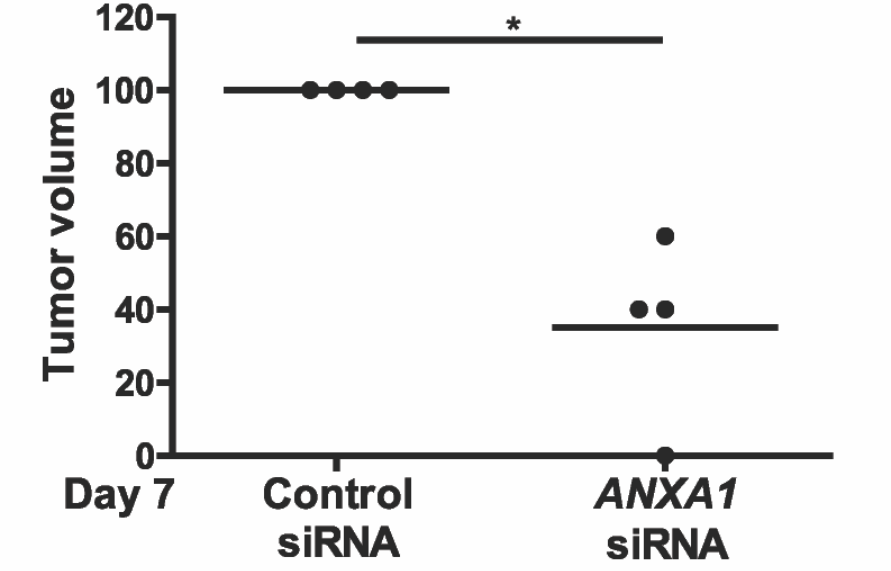
PDAC

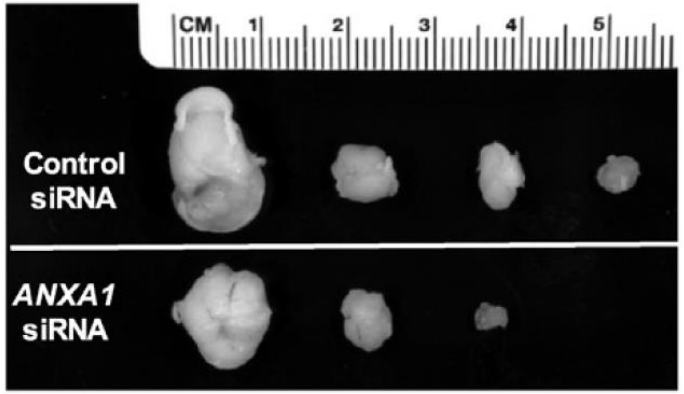


Rubinstein, M.R…… Han, Y.W. EMBO Reports 2019

In vivo validation

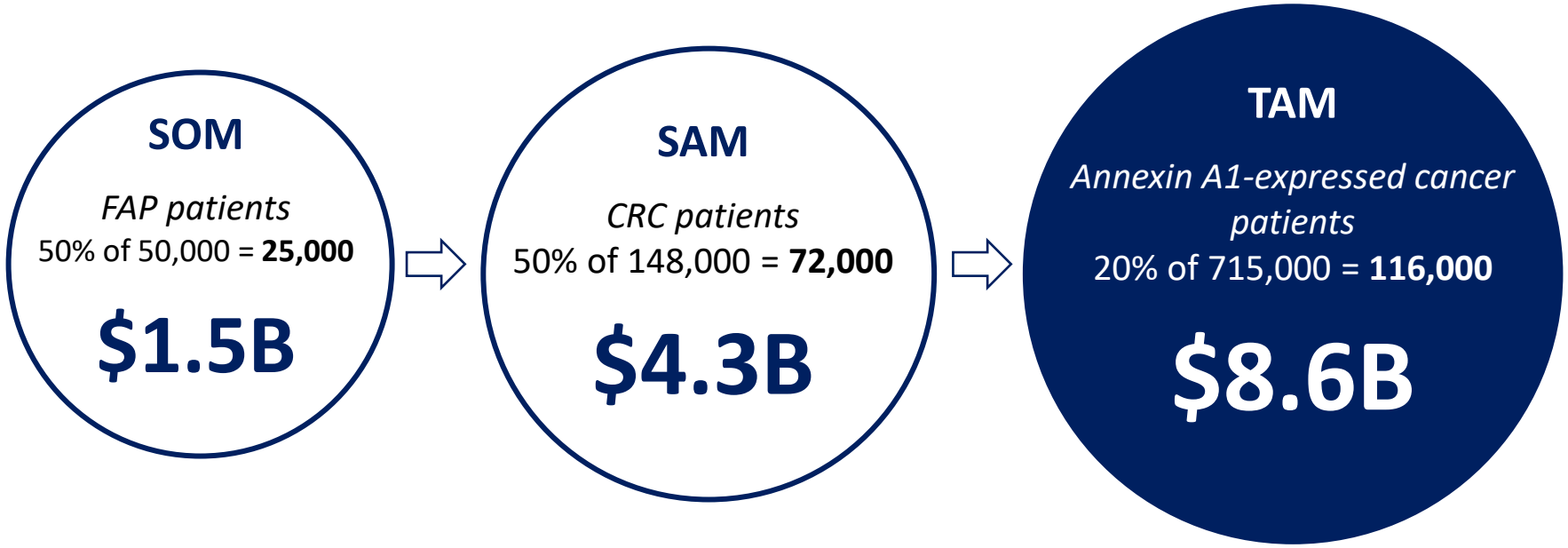
Inhibition of Annexin A1 by siRNA attenuates tumor growth in xenograft model





Rubinstein, M.R…… Han, Y.W. EMBO Reports 2019

U.S. Market Size



Priced at $60,000 annually

Competitive Landscape

EMTORA BIOSCIENCES

Commercializing eRapa™, a novel, targeted formulation of rapamycin

Small molecule targeting mTOR
Received $3M seed fund for Phase 2a in 2019

DNAlite

Gene therapy
Received $1.5M seed fund in 2018

janssen
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Anti-IL23 monoclonal antibody
Phase 1

- mTOR & IL 23 are not specific to polyps
- Gene therapy is new and complex
- Our approach is better targeted

External Validation

- Preclinical-stage biopharma company based in Edinburg, Scotland developing anti-ANXA1 mAb as cancer therapeutic
- Published work validates our science and does not cover FAP as an indication

Medannex

Value Proposition

- No effective therapy for FAP
- Targeted therapy reduces risk of off-target effects
- Significant value to delay colectomy at a young age
- Potential applications in other oncology indications

  Including pancreatic, liver, lung, bladder, endometrial, and melanoma cancers

Regulatory Strategy

Key Regulatory Parameters	Antibody Therapy for FAP
FDA Center for Review	Center for Drug Evaluation & Research (CDER)
Type of Applications	Investigational New Drug (IND) New Drug Application (NDA)
Drug Development Designations	**Orphan designation: qualifies for Orphan Drug Act** • Fast tracked for regulatory approval (6 months) • Waiver of prescription drug filing fees • Access to RO1 grants for orphan drug research • 7 years of marketing exclusivity • Tax credits for clinical research expenditures

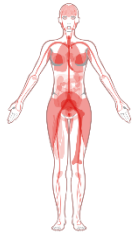
Recent Successes in Orphan Oncology

Acquired by Celgene for $7 billion in 2018, for fedratinib to treat myelofibrosis (~5,000 cases in US)

Acquired by Roche for $1.7 billion in 2017, during Phase 2 trial of entrectinib for NTRK solid tumors (1,500-5,000 cases in US)

Acquired by Astellas Pharma for $1.4 billion in 2016, following positive Phase 2b trial to treat advanced gastric cancer (27,000 cases in US per year)

Milestone Experiments



Evaluate Annexin A1 expression levels in FAP patients

(manuscript submitted for publication)

Test efficacy of monoclonal antibodies in xenograft and *Apc*$^{min/+}$ mice (manuscript submitted for publication)

Lead optimization, characterization, and candidate selection ~ six to nine months

Intellectual Property

Detection of Serum Anti-FadA Antibodies and Related Diagnostic Methods

US Application Filed May 2018

Methods for Treating, Preventing and Detecting the Prognosis of Colorectal Cancer

US Application Filed May 2019

Provisional patent application on matter of composition

Filed in April 2021

Founder & Management

Yiping Han, PhD
Founder, Professor and Chief Scientist

Mark Tang, PhD, MBA
Chief Executive Officer

Dan Luo, MD, PhD
Chief Operating Officer

Advisors & Consultants

Timothy Wang, MD
Chief of Gastroenterology
Columbia University

Fay Kastrinos, MD
FAP Specialist
Columbia University

Christina Mayer, Pharm D
Consultant for Pharmacological Studies

Peter Farina, PhD
Former SVP at Boehringer Ingelheim

Lan Huang, PhD
Founder and CEO
BeyondSpring Inc.

Mark Chiu, PhD
COO, Tavotek Therapeutics
Former Head, Process Analy. Sci., Janssen

Summary

- Targeting a novel protein to inhibit the growth of polyps in adolescents and young adults with FAP
- Development timeline reduced with Orphan Indication
- High unmet need
- Significant clinical and quality of life impact in delaying/preventing colectomy in young people
- **Potential additional indications – lung, colorectal, liver, pancreatic, melanoma, endometrial cancers etc.**