



celimmune

AMG 714, an anti-IL-15 antibody in development for the treatment of Celiac Disease and Refractory Celiac Disease Type II

Francisco Leon, MD PhD

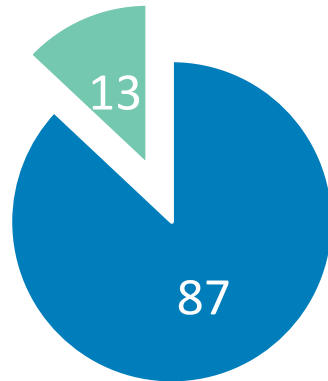
Disclosures

- Co-founder, former CEO/CMO, Celimmune LLC
 - Since end of 2017, a wholly owned subsidiary of Amgen Inc
 - Consultant, Amgen Inc
- Former CMO, Alba Therapeutics
- Partner, Biomedal SA
- Co-founder, director, Glutenostics LLC
- Co-founder, CSO, Provention Bio
- President, PharmImmune LLC



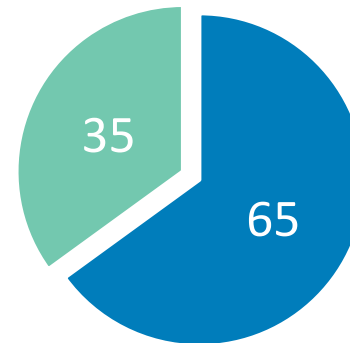
Celiac patients' attitudes regarding novel therapies

Want a Drug to Protect from Cross-Contamination (Adjunct to GFD)



■ Interested ■ Not Interested

Want a Drug to Enable Gluten Consumption (Replacement of GFD)

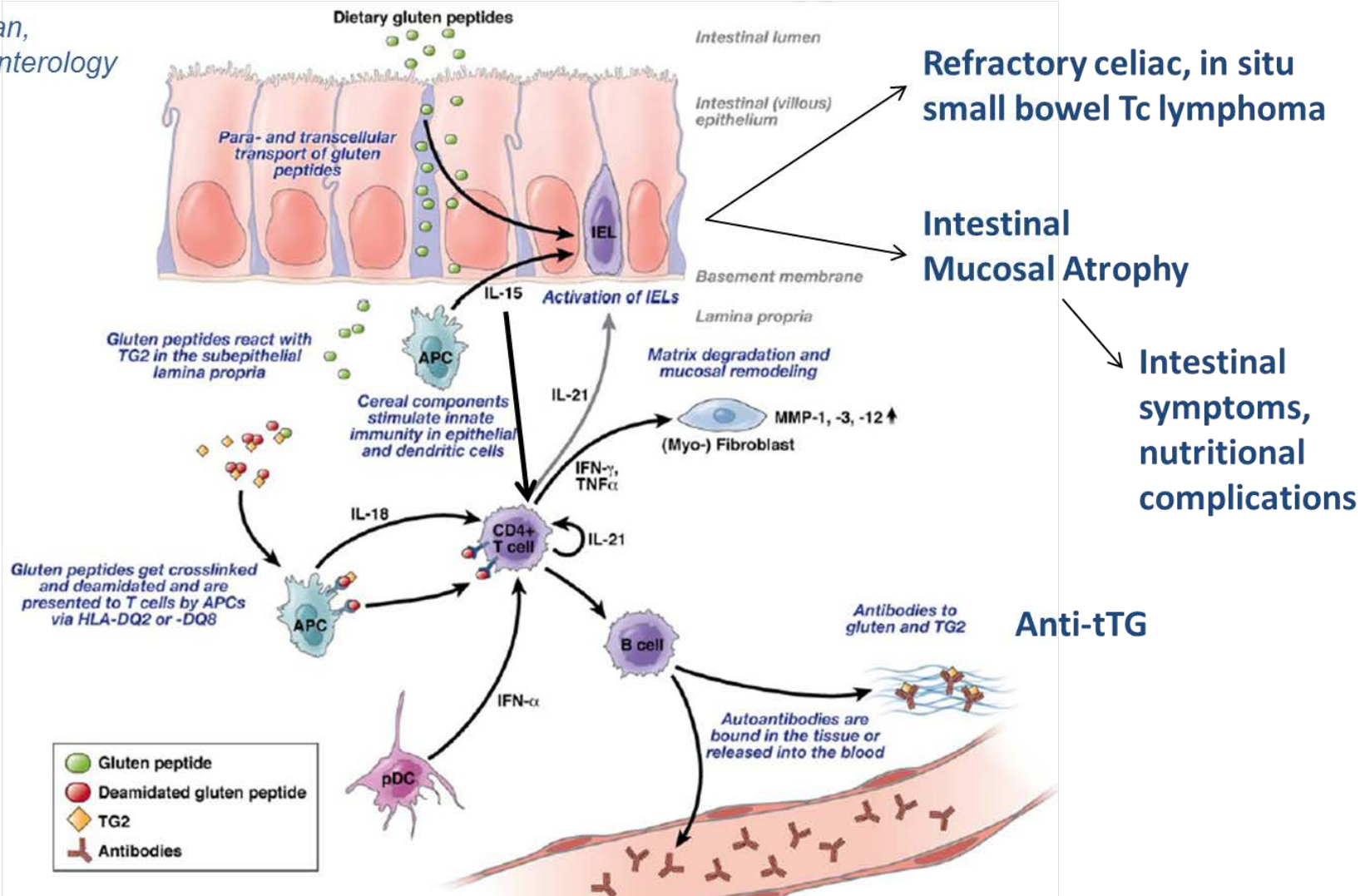


■ Interested ■ Not Interested

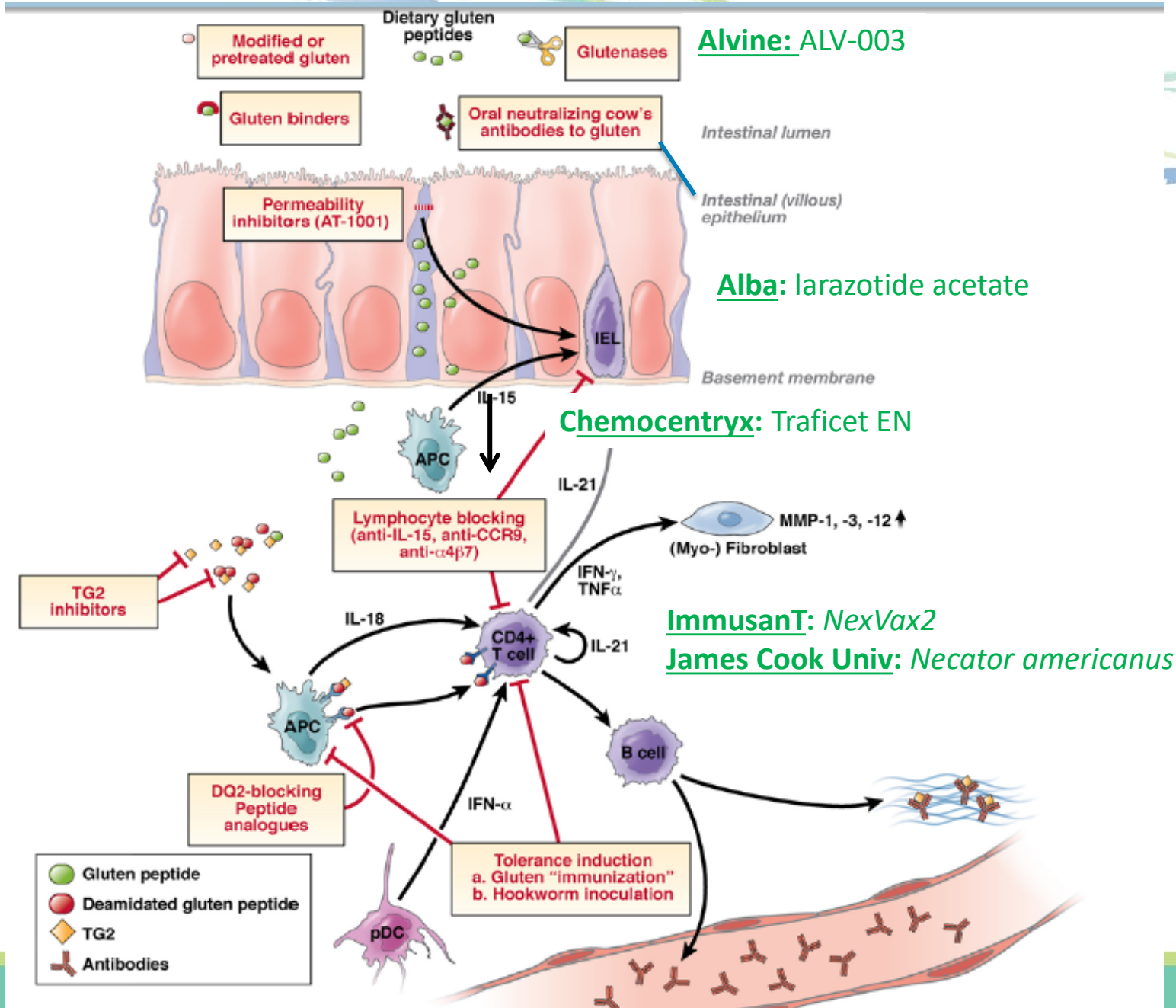
Tomal J, McKiernan D, Guandalini S, Semrad CE, Kupfer SS. Celiac patients' attitudes regarding novel therapies. Minerva Gastroenterol Dietol 2016;62:275-80

CeD Pathogenesis and Therapeutic Targets

Schuppan, Gastroenterology 2009



Experimental non-dietary therapies for celiac disease (2010)



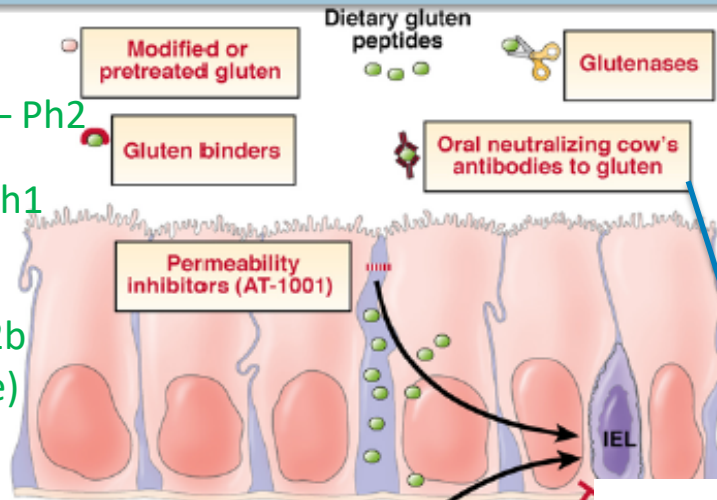
Experimental non-dietary therapies for celiac disease (2018)

Universities: Modified G

Probiotics – Ph2

BiolineRx: **BL-7010** – Ph1

Innovate: – **INN-202** – Ph2b
(formerly Alba's larazotide)



ImmunogenX: **Latiglutenase/IMGX-003**
(formerly Alvine's ALV-003) – Ph2b

Allergan: **Viokase/pancrelipase** – Ph2a

PvP Biologics: **KumaMax**

Pre-clinical (Takeda)

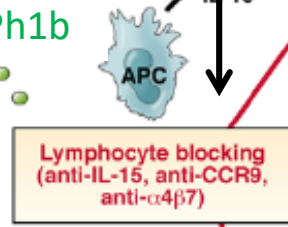
IGY Life Sciences: **IgY** – Ph1/2

Chicago Celiac Center: **Montelukast** – Ph1b

Zedira/Falk Pharma: **ZED1227** – Ph2a

Sitari: Pre-clinical tTG inhib (GSK)

UCB: Pre-clin tTG inhibitor



Celimmune: **AMG 714** – Ph2a (Amgen)

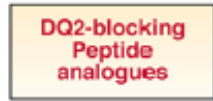
Mayo Clinic/NCI: **HuMikβ1** – Ph2a

Calypso: **CALY 002** – Pre-clinical (Merck KGa)

Bioniz: **BNZ-2** – Pre-clinical (Takeda)

Takeda: **Vedolizumab/ENTYVIO** – Ph1b

Provid: Pre-clinical



ImmusanT: **NexVax2** – Ph2a

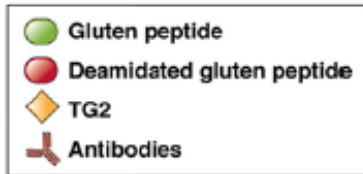
James Cook Univ: **Hookworm NainCeD-3** – P1b

Cour: **NP-GLI** – Ph1b – (Takeda)

Kanyos Bio: Pre-clinical (Astellas/Anokion/Celgene)

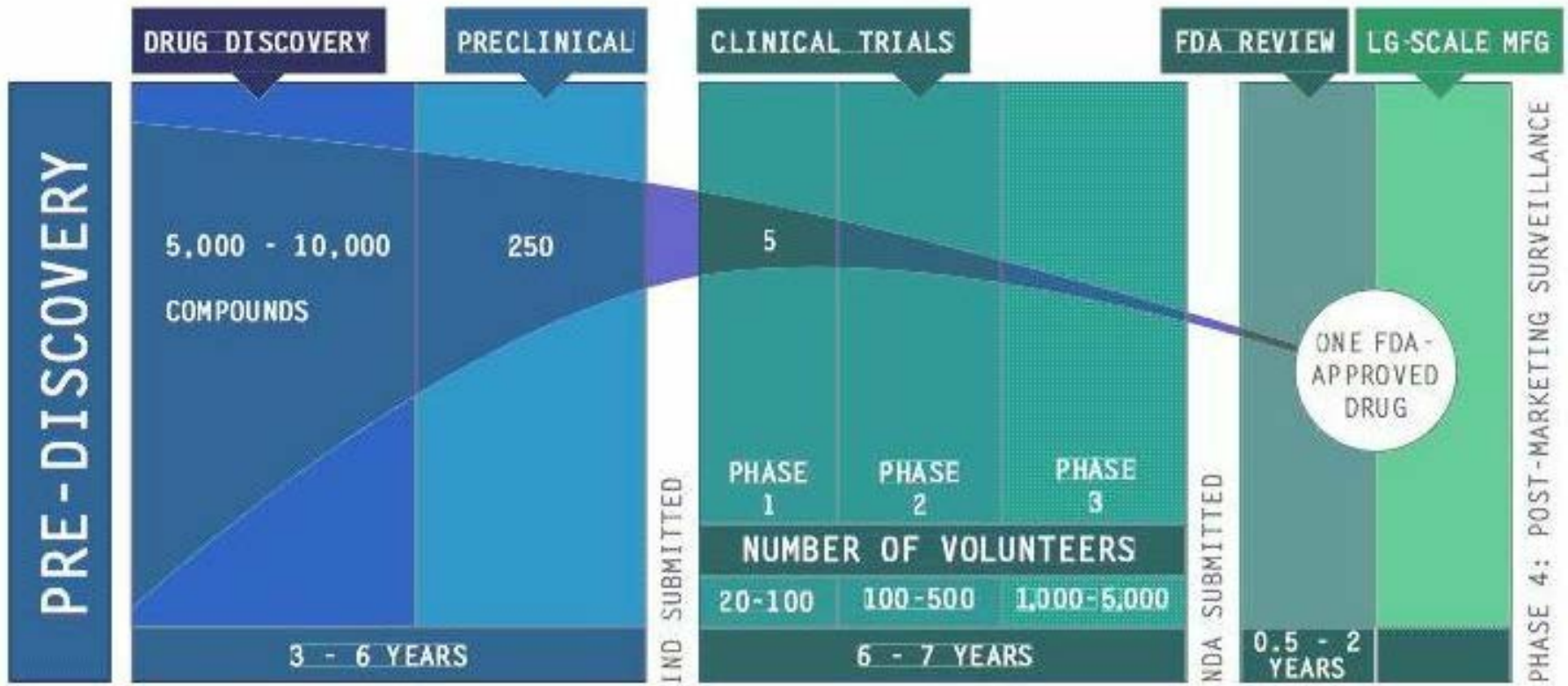
Topas: Pre-clinical (Lilly)

Selecta: Pre-clinical

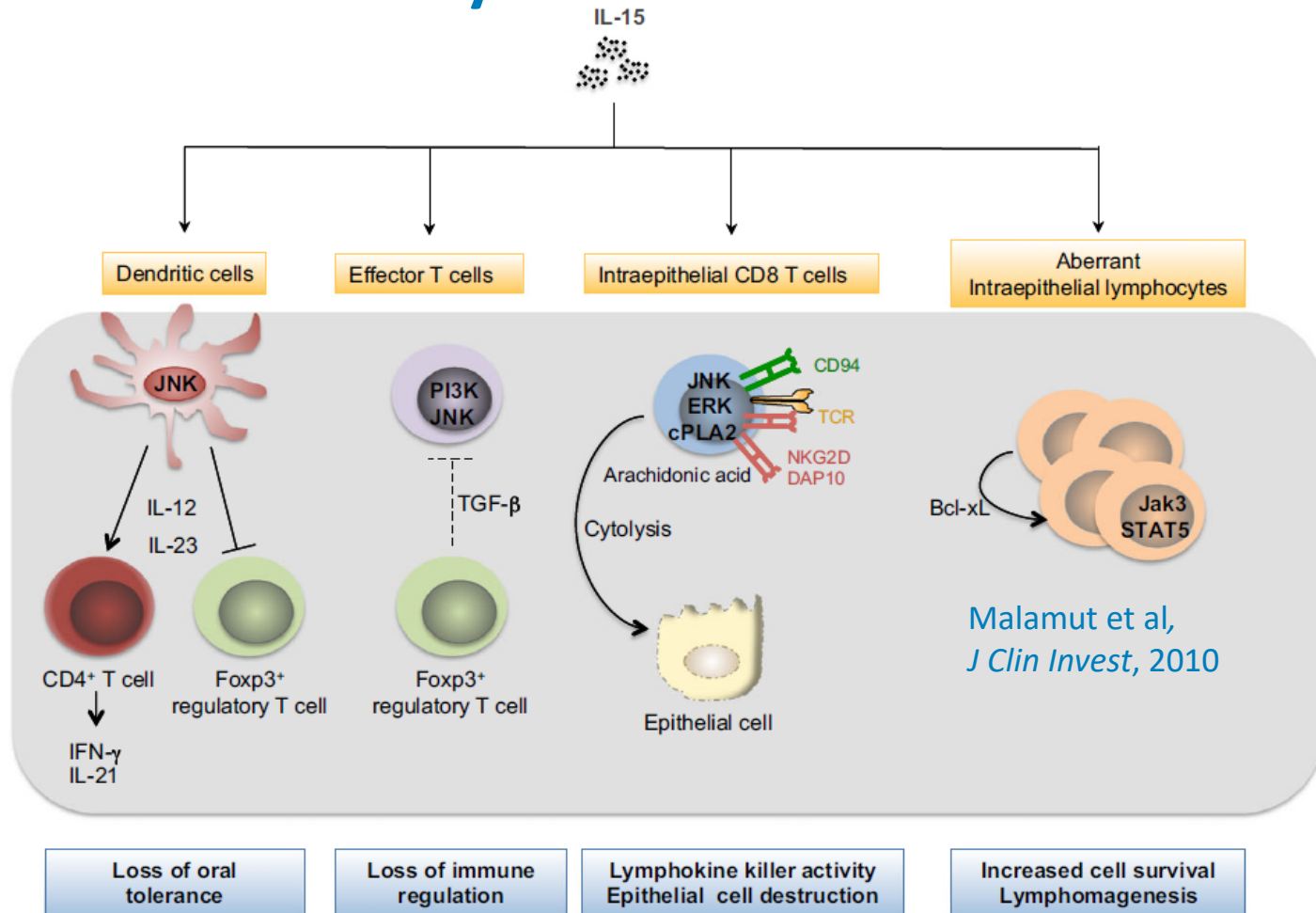


We need multiple shots on goal

since: 1) most experimental medicines fail to be approved
2) it's likely that combinations will be needed



IL-15 is a central regulator in celiac and refractory celiac disease

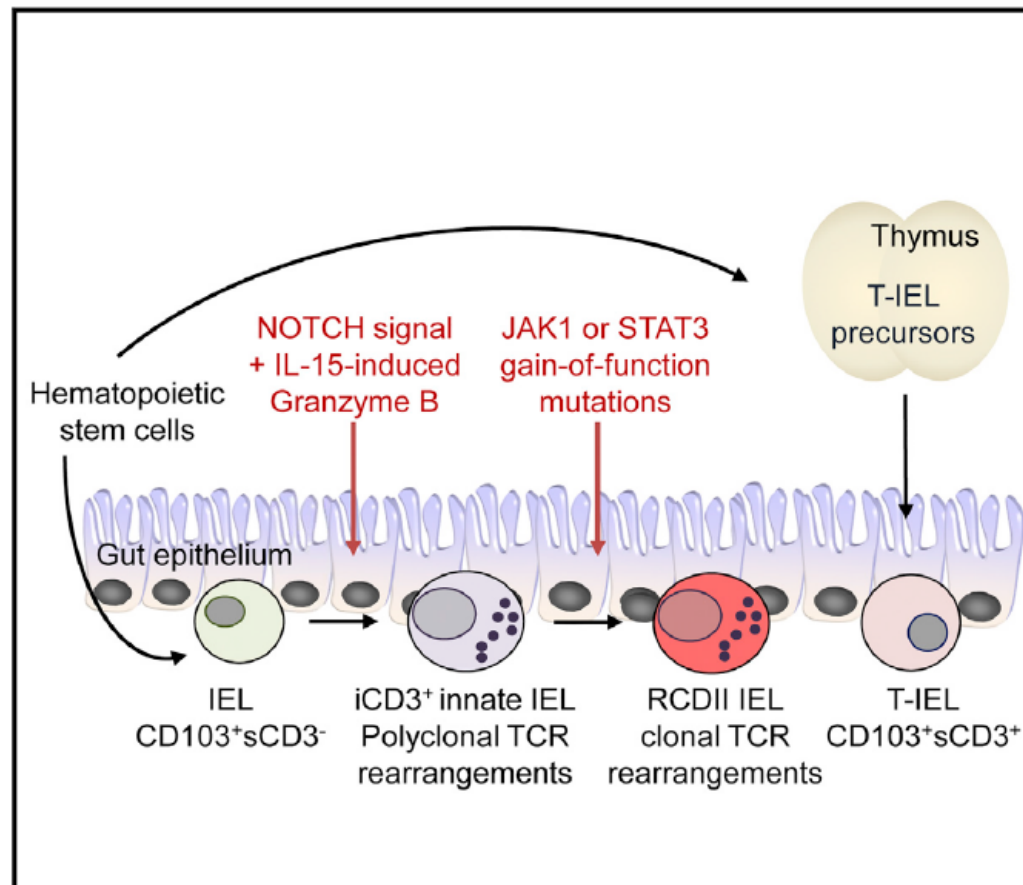


Abadie, Jabri: "IL-15: a central regulator of celiac disease immunopathology". *Immunol Rev*, 2014

Immunity

Interleukin 15-Dependent T Cell-like Innate Intraepithelial Lymphocytes Develop in the Intestine and Transform into Lymphomas in Celiac Disease

Graphical Abstract



Authors

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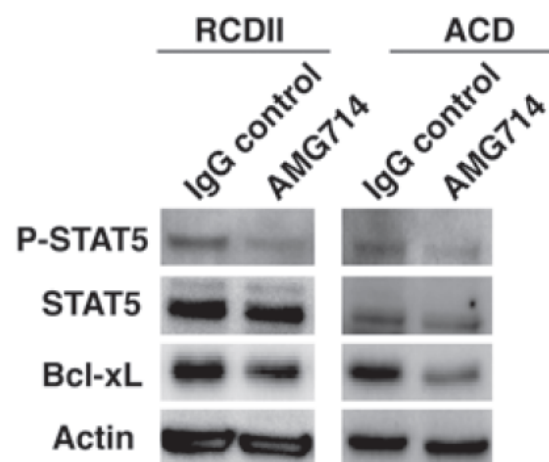
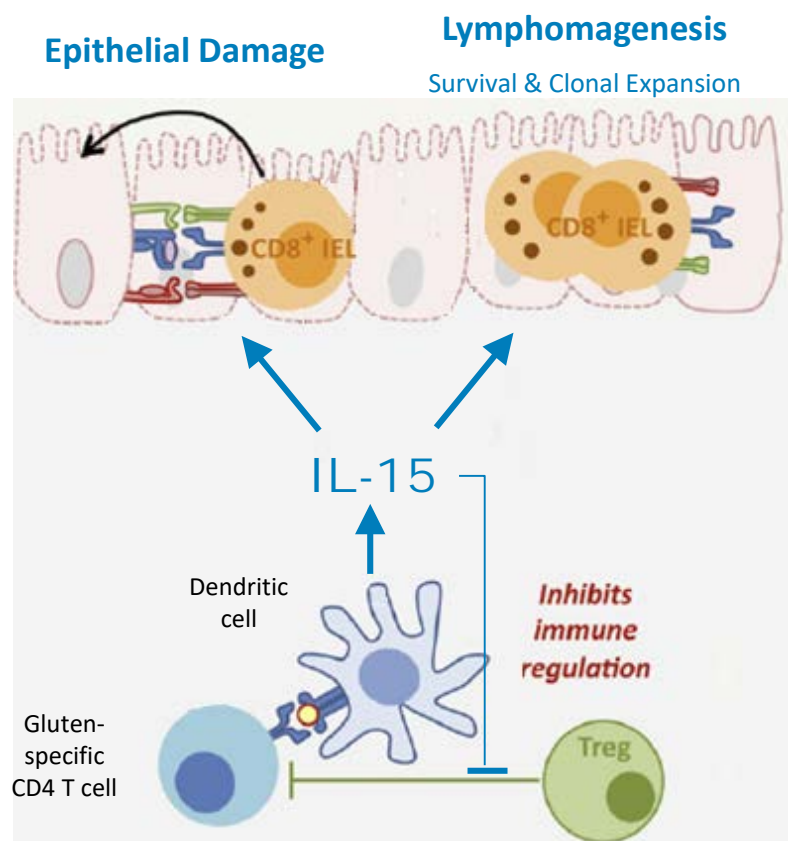
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In Brief

Ettersperger, Montcuquet et al. showed that innate lymphocytes with T cell traits were present in the gut epithelium. The latter cells differentiated independently of Id2 in response to NOTCH and IL-15 signals. They acquired gain-of-function

AMG 714 efficacy in celiac models

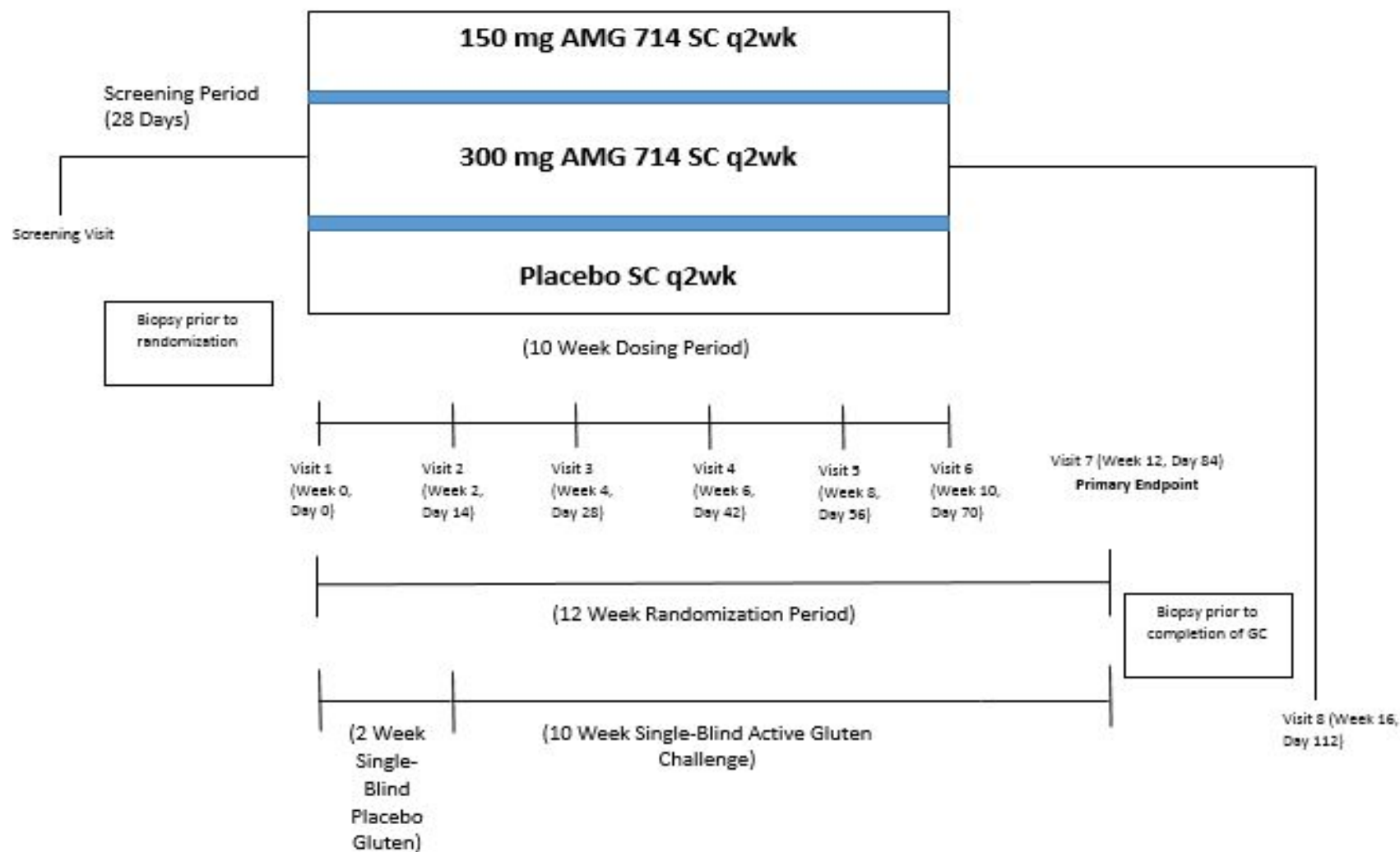
AMG 714 induces apoptosis of IELs in Active Celiac and RCD II explants



Malamut *et al.* "IL-15 triggers an antiapoptotic pathway in human intraepithelial lymphocytes that is a potential new target in celiac disease-associated inflammation and lymphomagenesis." *J Clin Invest* 2010

CELIM- NRCDD-001: Gluten Challenge study of AMG 714 to test potential in GFD Non-Responsive Celiac Disease

Finland (Maki): Tampere (Lähdeaho), Turku (Scheinin), Oulu (Vuotikka)



Measuring gluten immunogenic peptides (GIP) facilitates the conduct of celiac clinical trials and helps self-monitoring of the GFD by patients



Biomedal

iVYLISA GIP

*ELISA format for
Research & Local Labs*

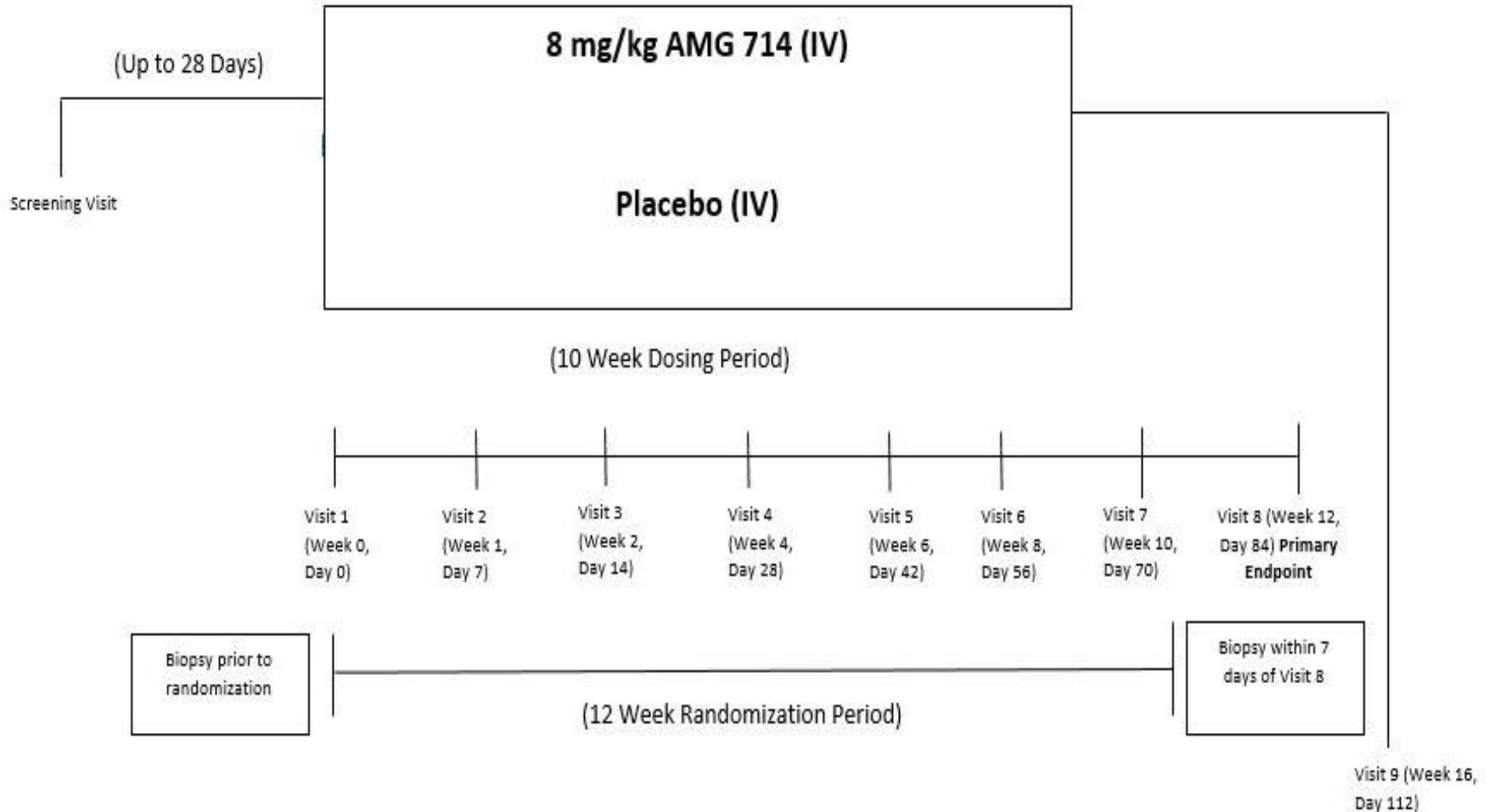
Gluten
DETECTIVE



*Lateral Flow ImmunoAssay (LFIA) for
Point-Of-Care Testing (POCT) &
Over the Counter (OTC)*

CELIM-RCD-002: AMG 714 to treat RCD-II/Pre-EATL

San Diego (Crowe...), NYC (Green, Bhagat, Vlad...), Paris (Cellier, Cerf-Bensussan...), Amsterdam (Mulder, Bouma, Van Gils, Lundin, Sanders...), Tampere (Collin...), Madrid (Crespo...)



THANK YOU TO THE NRCD-001 INVESTIGATORS AND COORDINATORS

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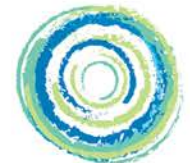
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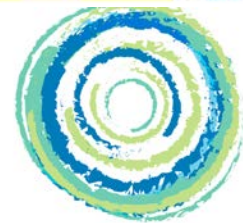
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- **UCSD (San Diego)**
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 - Christophe Cellier, Sherine Khater, Georgia Malamut,
 - Nadine Cerf-Bensussan, Bertrand Meresse (Institute *Imagine*)
- **VU University Medical Center (Amsterdam)**
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 - Knut Lundin, Valerie Byrnes, David Sanders, Michael Schumann
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