



SEARCH FOR A POTENTIALLY PREDICTIVE GLYCOBIOLOGICAL SIGNATURE OF THE TRANSITION FROM ULCERATIVE COLITIS TO COLITIS-ASSOCIATED COLORECTAL CANCER

Final Engineering Project — Bachelor of Biotechnology



Lucía Castelli — 2025

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Dr. Mariño, Karina

UADE

Universidad Argentina de la Empresa (UADE)
Functional and Molecular Glycomics Laboratory
Institute of Biology and Experimental Medicine – IBYME

CONICET

CONICET



I B Y M E



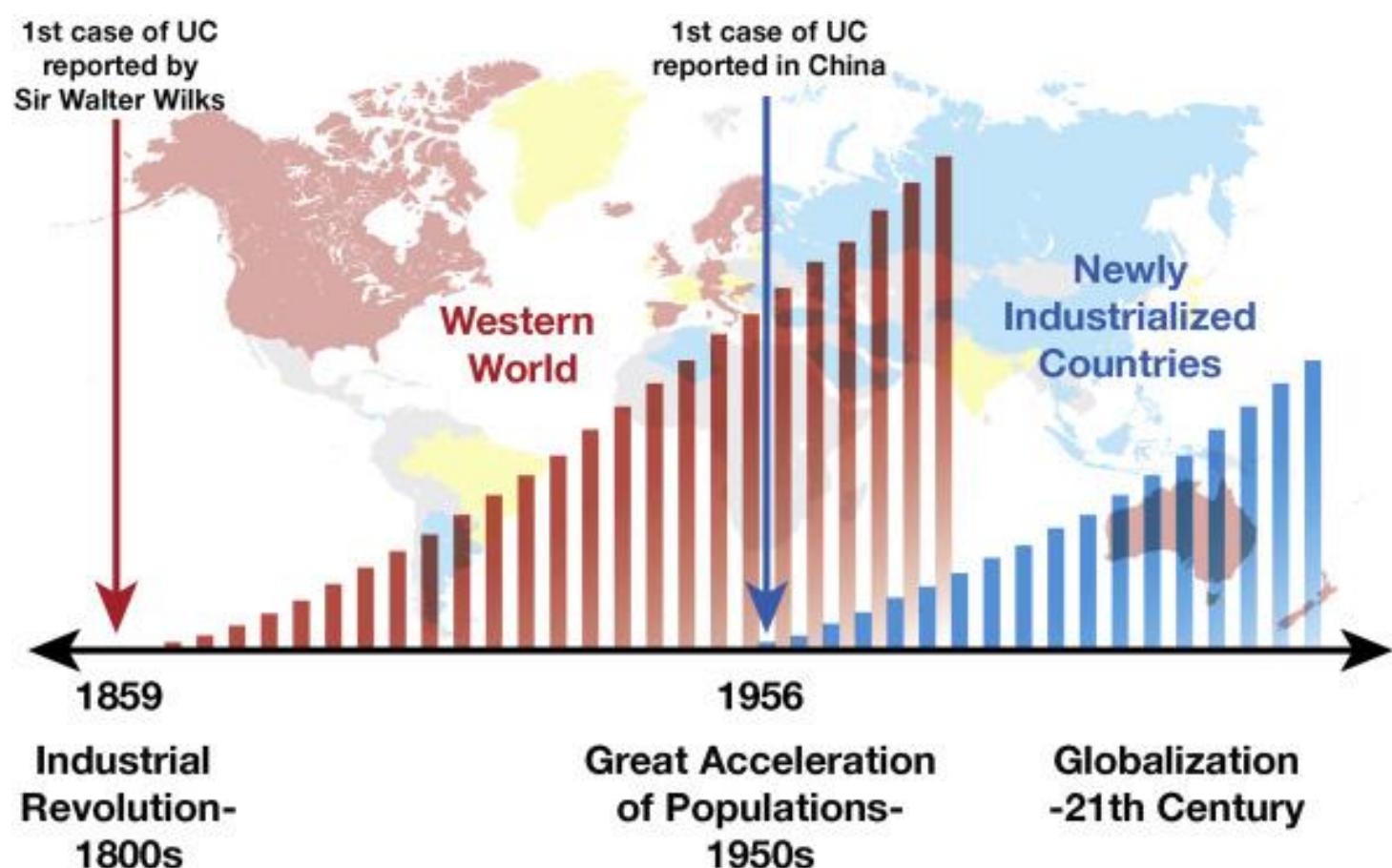
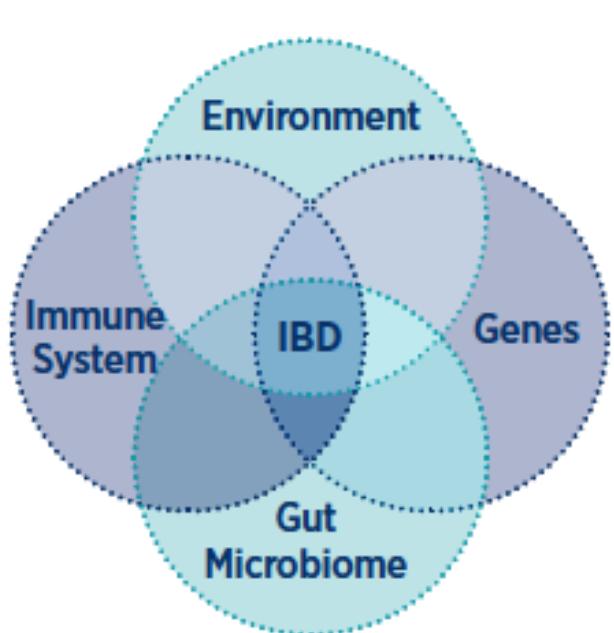


INTRODUCTION: BACKGROUND

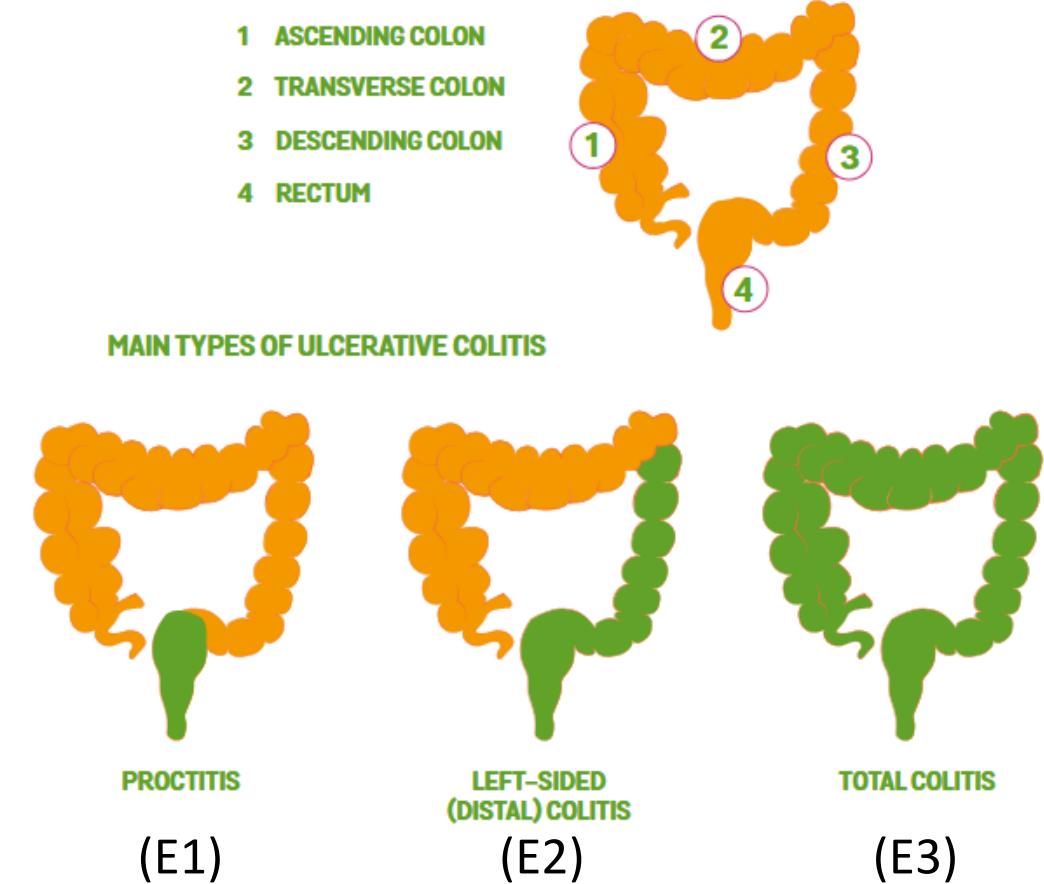
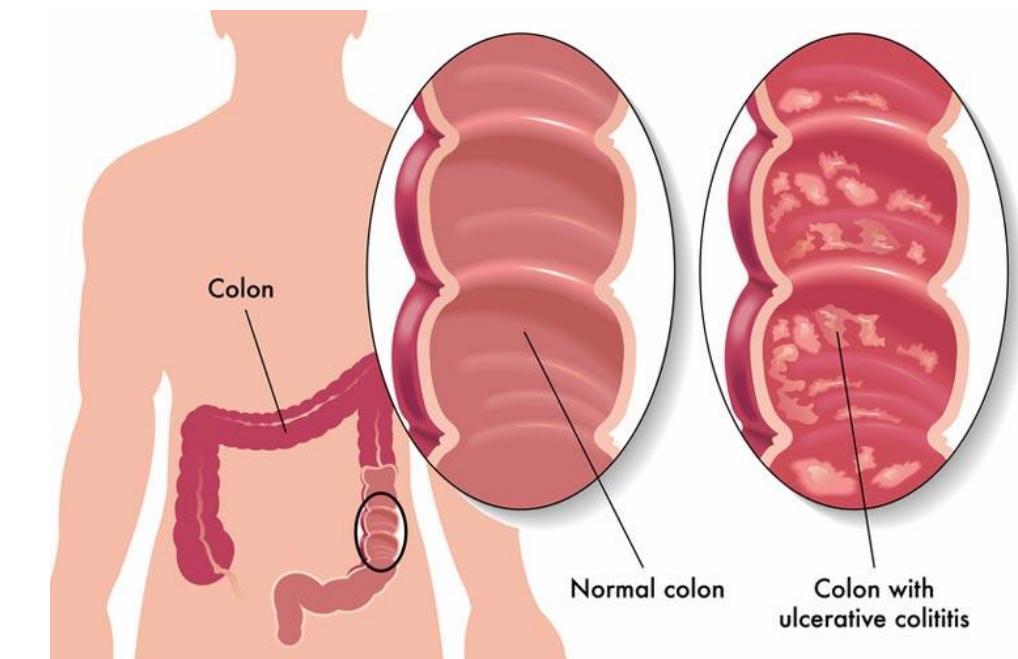
INFLAMMATORY BOWEL DISEASES

 **About Inflammatory Bowel Disease (IBD)**
Information from the American College of Gastroenterology on Ulcerative Colitis and Crohn's Disease

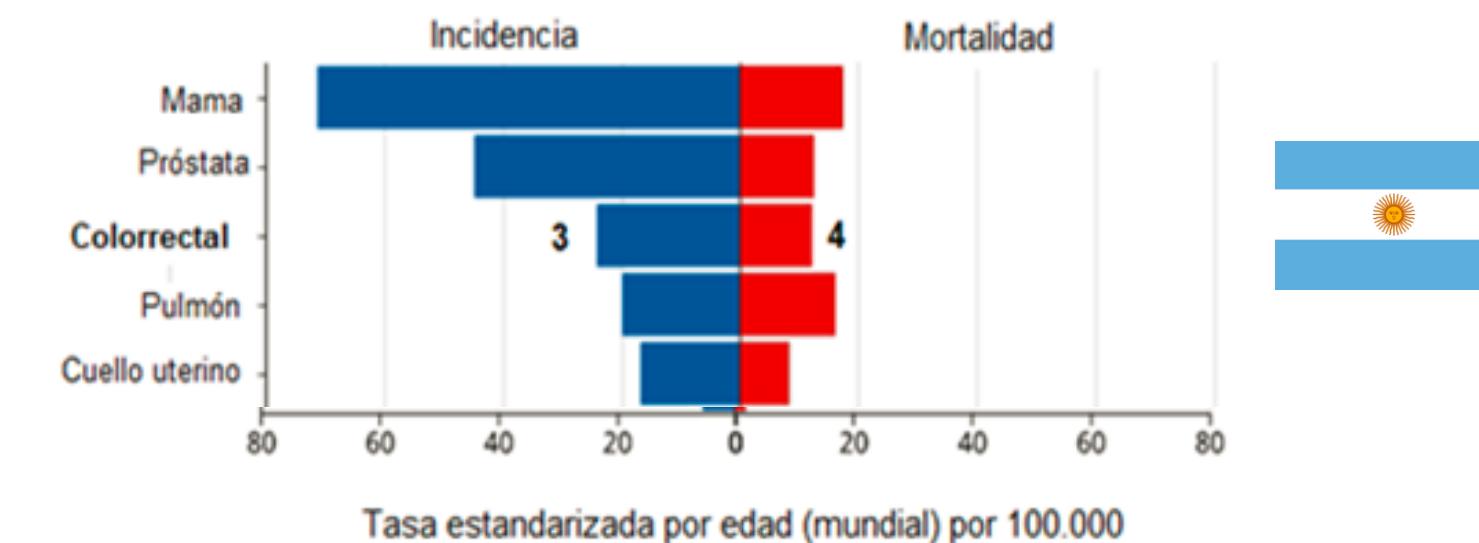
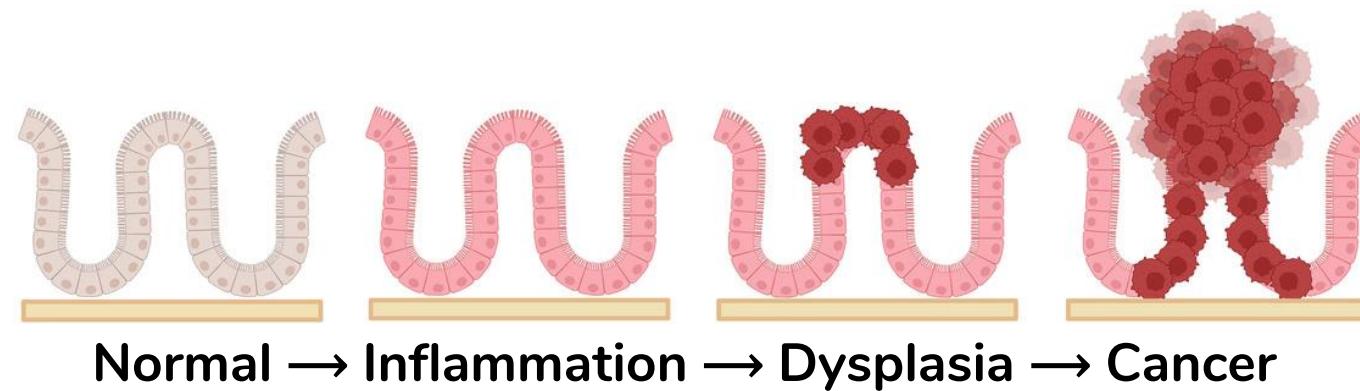
INFLAMMATORY BOWEL DISEASE (IBD) is an umbrella term for the chronic gastrointestinal inflammatory conditions ulcerative colitis and Crohn's disease.



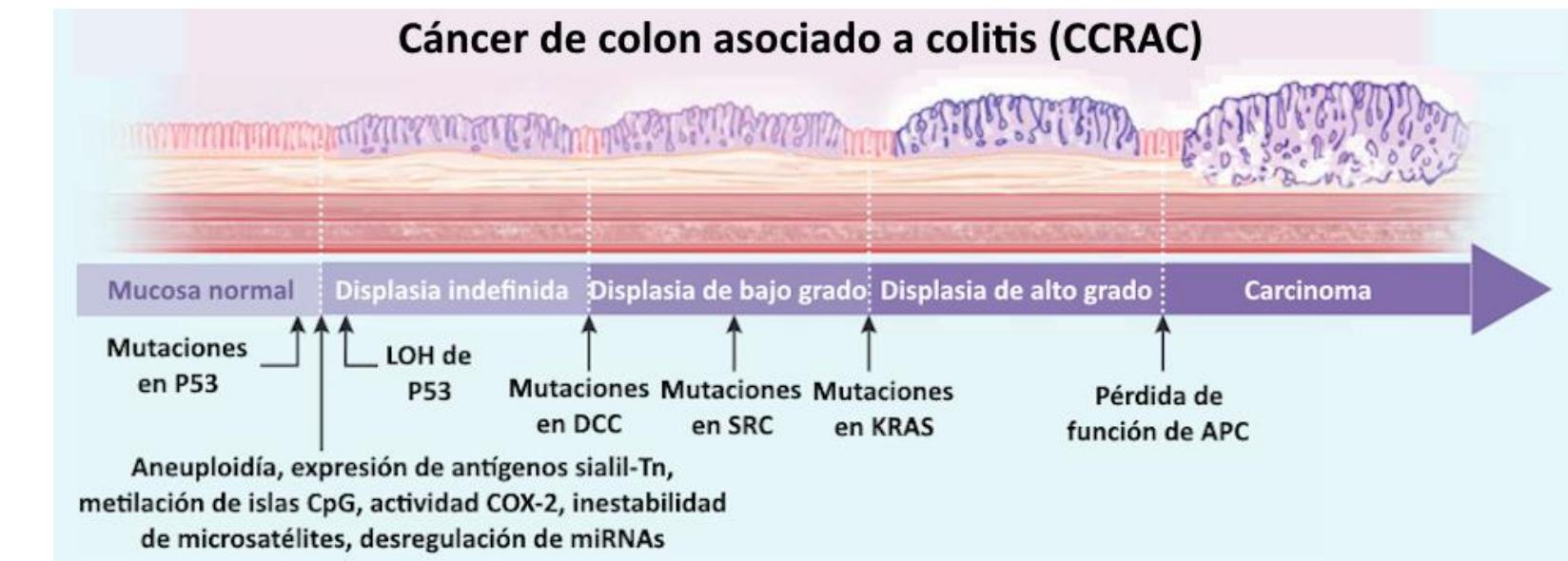
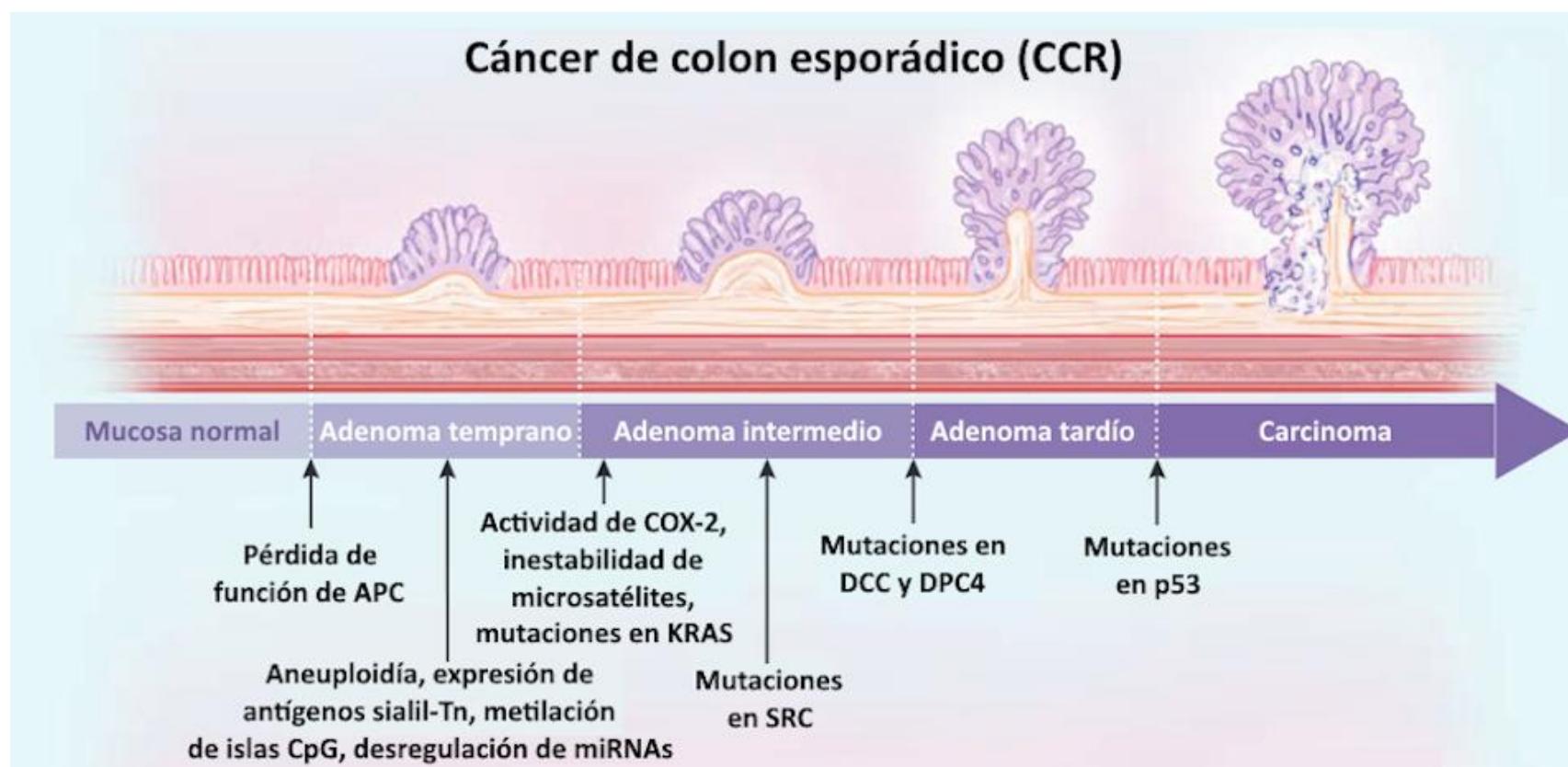
Kaplan et al (2017). Understanding and Preventing the Global Increase of Inflammatory Bowel Disease.



SPORADIC COLORECTAL CANCER ASSOCIATED WITH COLITIS

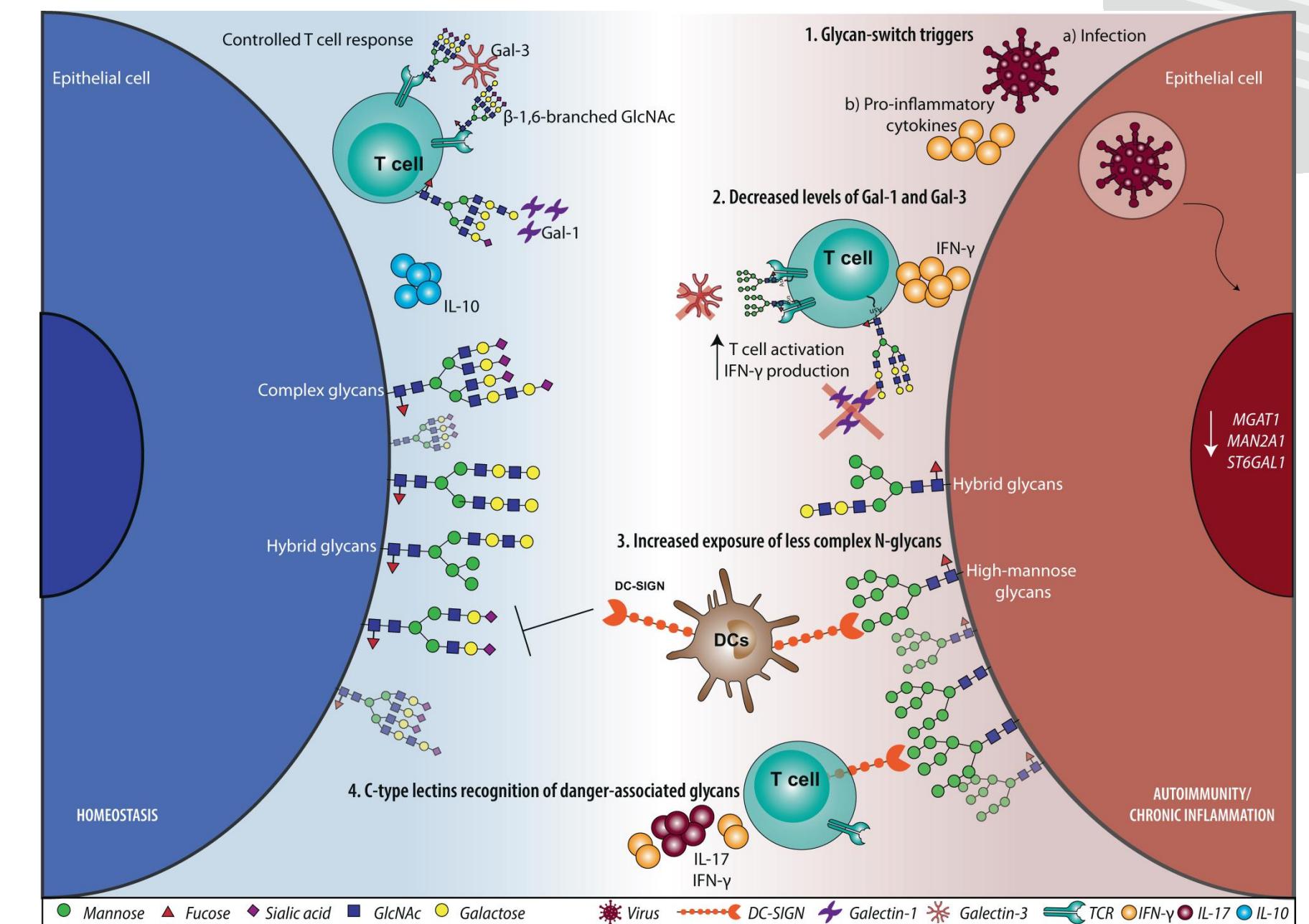
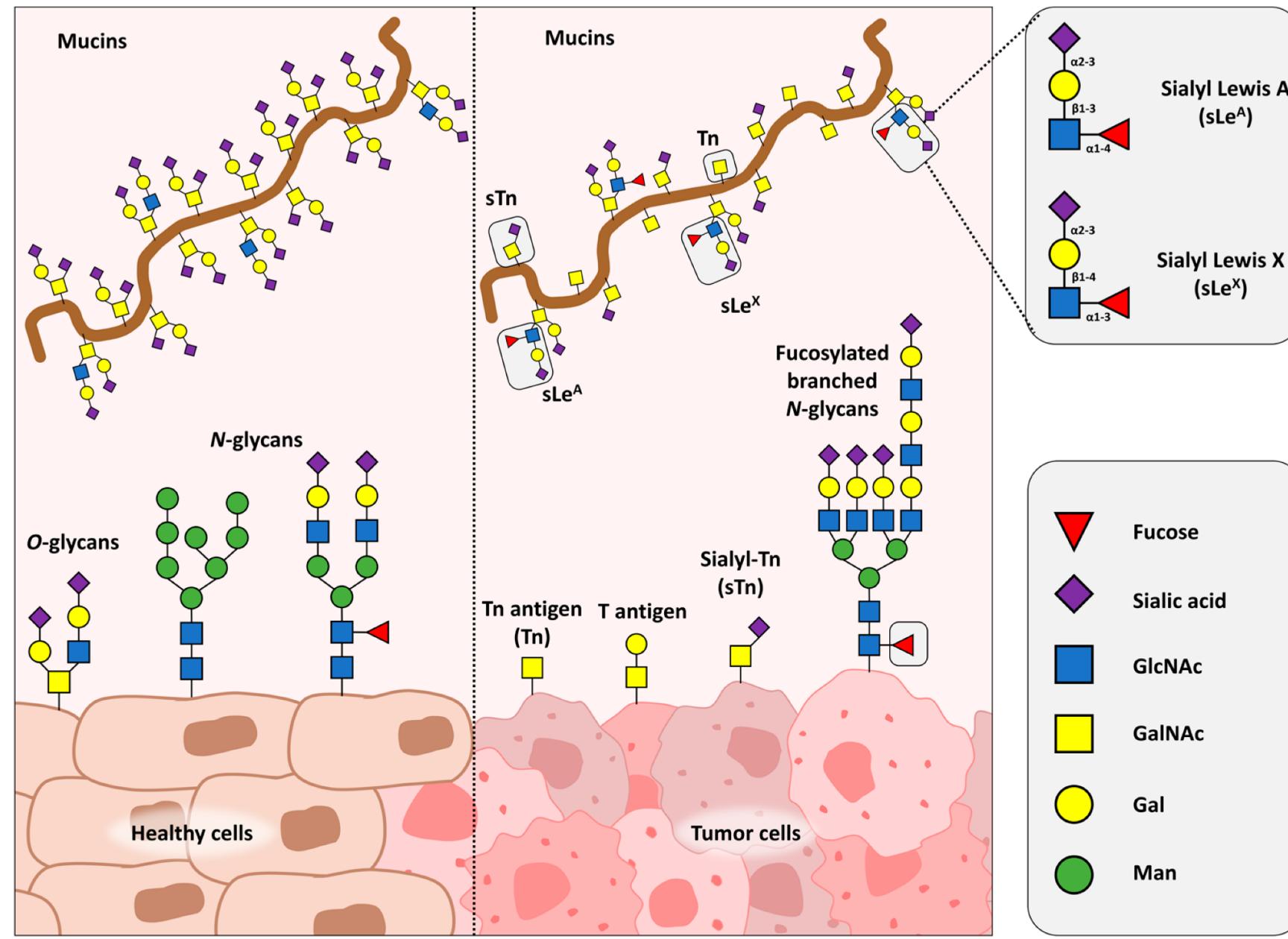


Ferlay, et al. (2024). Cancer today – : <https://gco.iarc.who.int/today/>



Beaugerie e Itzkowitz (2015). Cancers Complicating Inflammatory Bowel Disease. Doi: 10.1056/NEJMra1403718

GLYCOBIOLOGY AS A TRANSVERSAL DISCIPLINE IN BIOMEDICAL SCIENCES



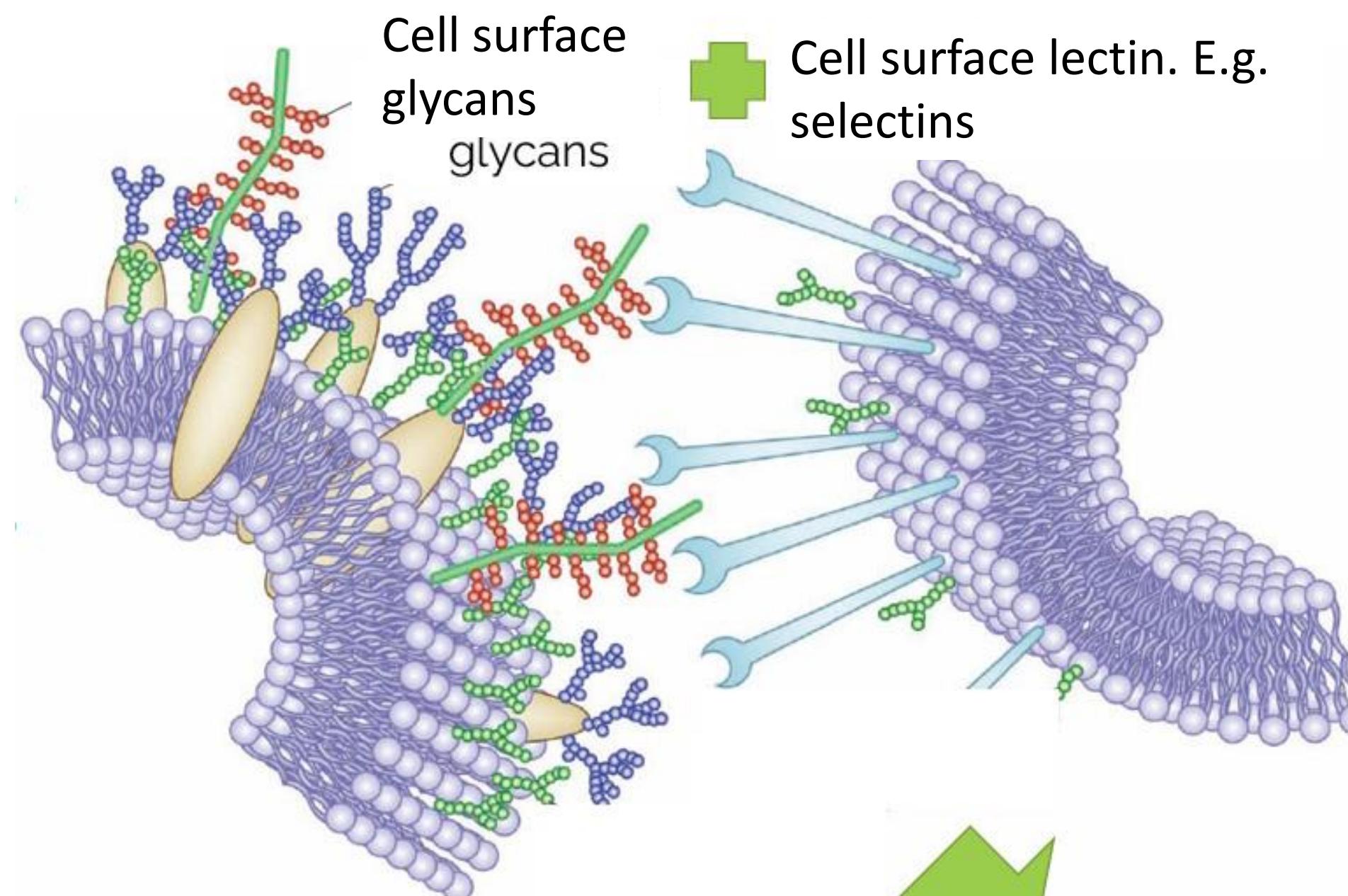
The Blessed Union of Glycobiology and Immunology: A Marriage That Worked, Medicines 2023

Immune regulatory networks coordinated by glycans and glycan-binding proteins in autoimmunity and infection, Pinho et al, Cell Mol Immunol 2023

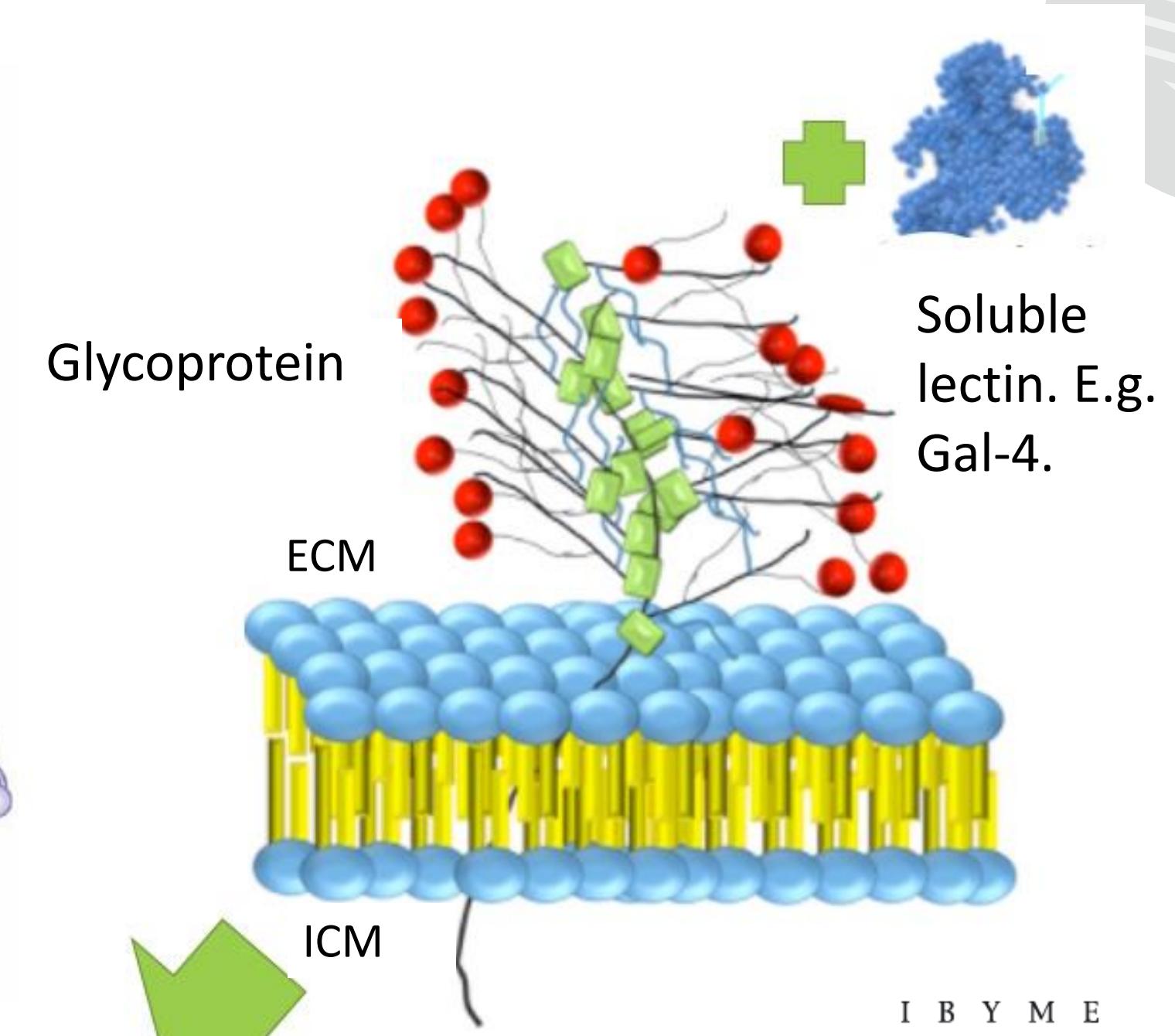


Background

LECTINS DECODE GLYCAN INFORMATION AND INITIATE IMMUNE RESPONSES



Cell surface lectin. E.g.
selectins



Glycoprotein

ECM

ICM

*Immunological
effects*

Nature Methods 8, 55–57 (2011)

IBYME
CONICET
IBYME

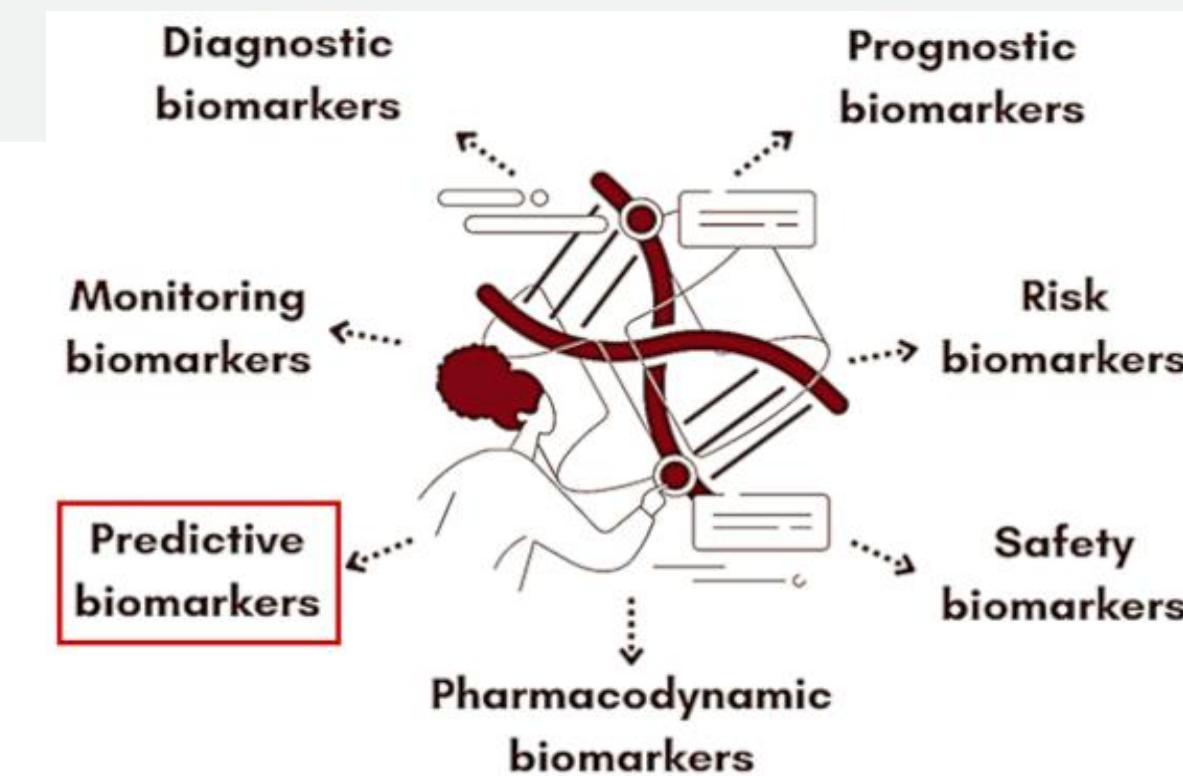
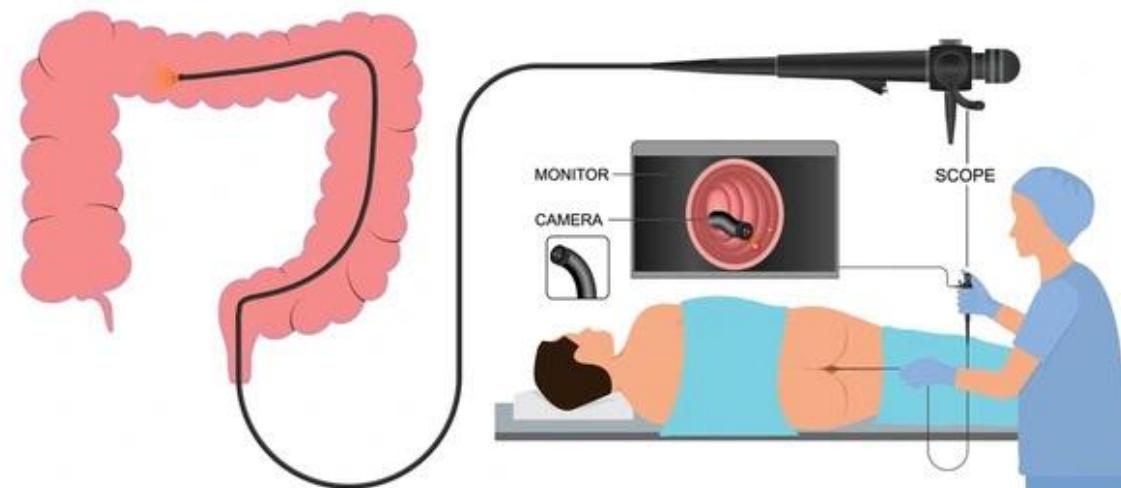
Background



HYPOTHESIS

HYPOTHESIS AND GENERAL OBJECTIVE

Glycogenes (related to glycosylation and lectins) could be dysregulated in neoplasm associated with intestinal inflammation, and their study would allow us to identify a signature of expression predictive of the development of neoplasia in these patients.





OBJECTIVES

SPECIFIC OBJECTIVES

#1

Develop and validate a glycogene signature based on samples from **patients** with ulcerative colitis (UC) and neoplasia.



#2

To comparatively analyze the glycogene signature obtained in UC with and without neoplasia in experimental **models** of colitis and CCRAC.



#3

Validate the expression profiles associated with the development of CCRAC in murine models by **RT-qPCR**



DEVELOPMENT OF BIOINFORMATICS TOOLS

Visualización de expresión diferencial

p-value

logFC

Up: 12, down: 7

Seleccioná los datos para mostrar:

Ejemplo (firma)

Subir .csv

C Refrescar tabla

Tabla Gráfico NCBI Más Información

An official website of the United States government [Here's how you know](#)

National Library of Medicine
National Center for Biotechnology Information

Gene Gene Defa5 Create RSS Save search Advanced

Gene sources Tabular 20 per page Sort by Relevance

Genomic Catego... Alternatively spliced Annotated genes Protein-coding Pseudogene

Seque... content CCDS Encyclohl

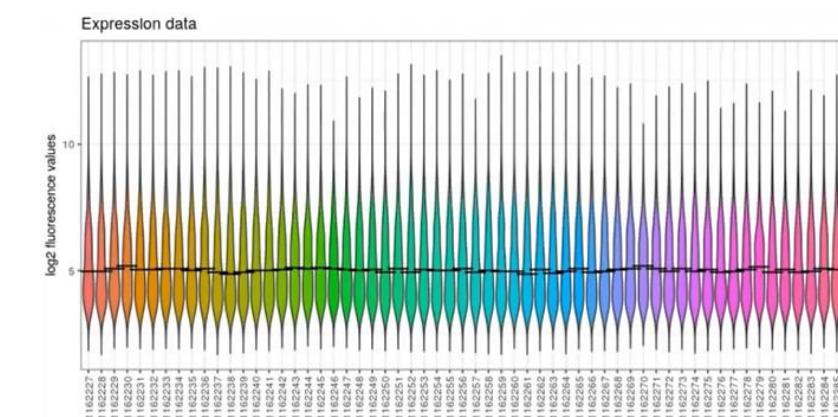
GENE Was this helpful?

DEFA5 – defensin alpha 5
Homo sapiens (human)
Also known as: DEF5, HD-5

<https://lcastelli.shinyapps.io/degs/>

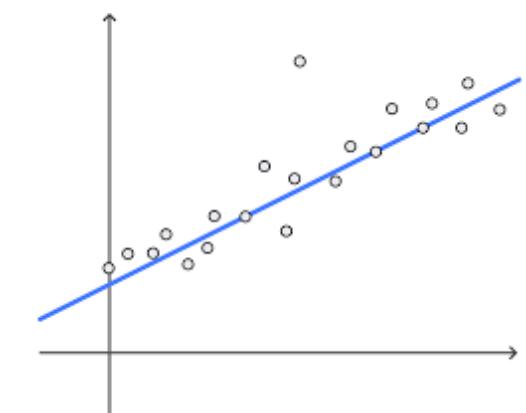
Degfind

R package for differential expression analysis in bulk (RNA-seq and microarrays). Eight (8) functions for raw data handling, QC, graphing, and statistical analysis.



```
> topTable(fit, coef=2, n=40, adjust="BH")
```

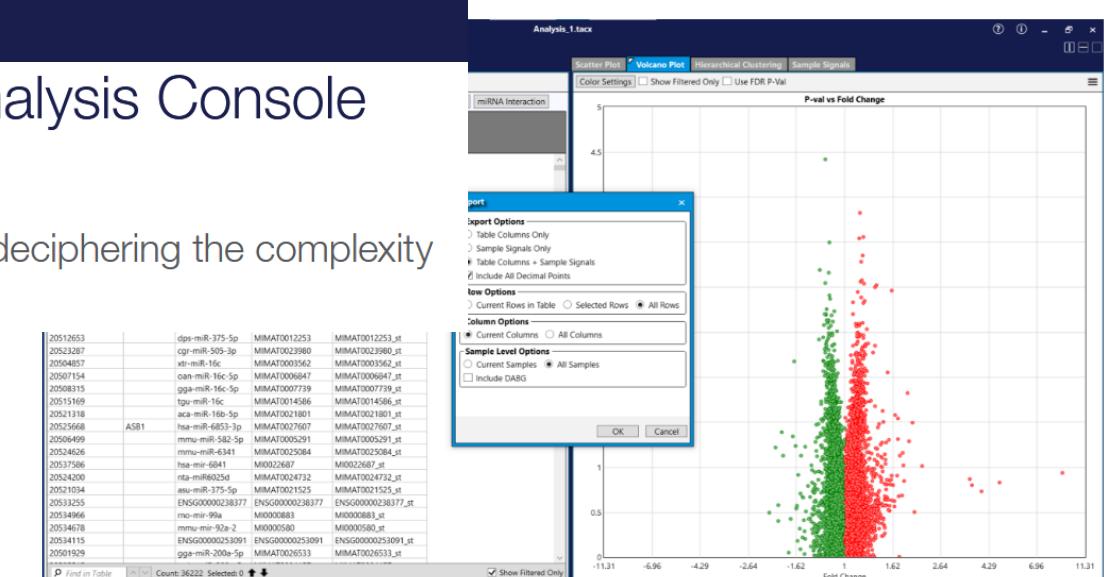
ID	logFC	AveExpr	t	P.Value	adj.P.Val	B
4282	IG_821_1300838_1300922_fwd_st	-3.32	12.4	23.1	7.2e-09	5.3e-05
5365	serA_b2913_st	2.78	12.2	15.8	1.6e-07	6.0e-04
1389	gltD_b3213_st	3.03	10.9	13.3	6.4e-07	1.6e-03
4625	lrp_b0889_st	2.30	9.3	11.4	2.3e-06	4.0e-03



applied**biosystems**

Transcriptome Analysis Console (TAC) Software

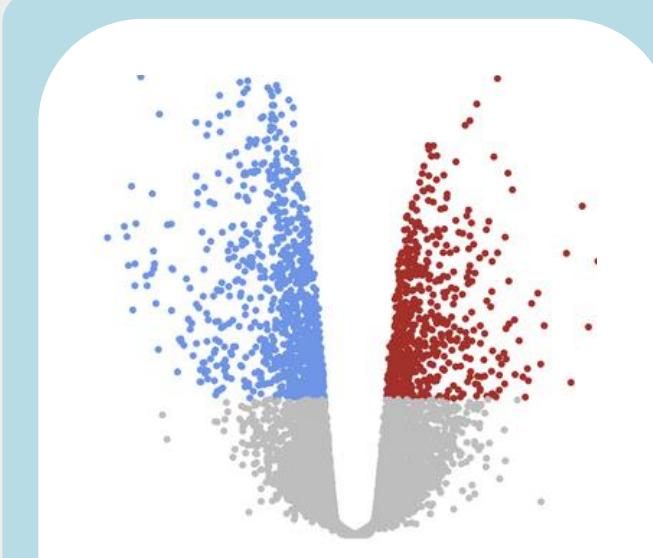
Fast, intuitive software for deciphering the complexity of the transcriptome



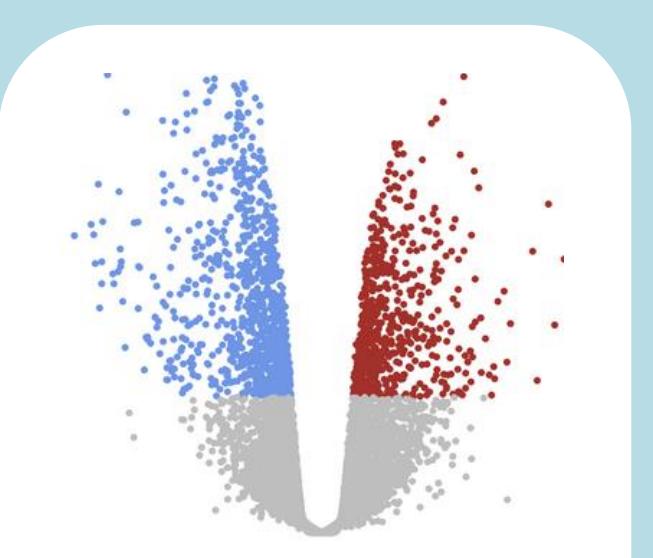
Introduction

EXPERIMENTAL DESIGN

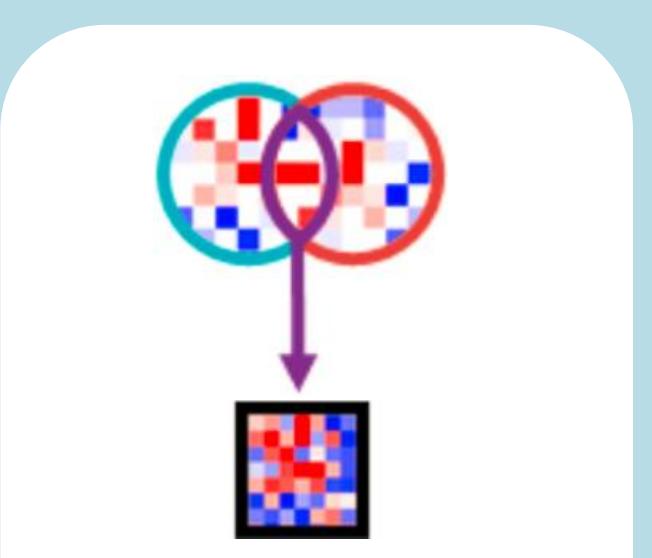
CU / Healthy



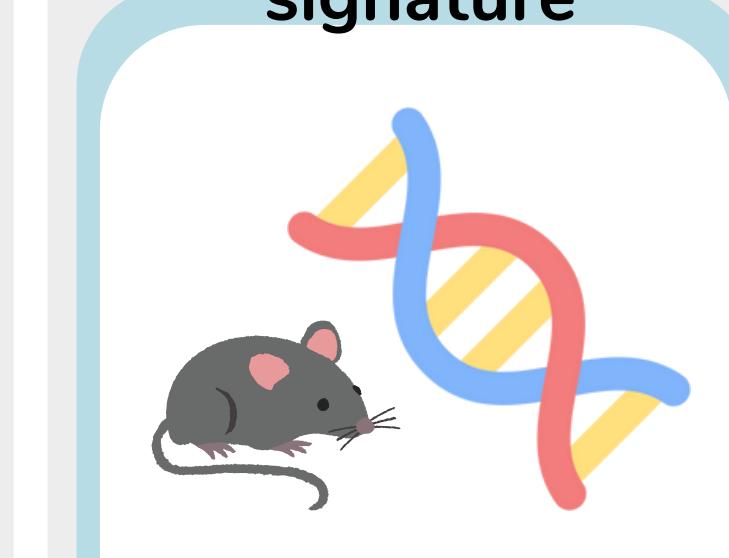
Displasia / CU



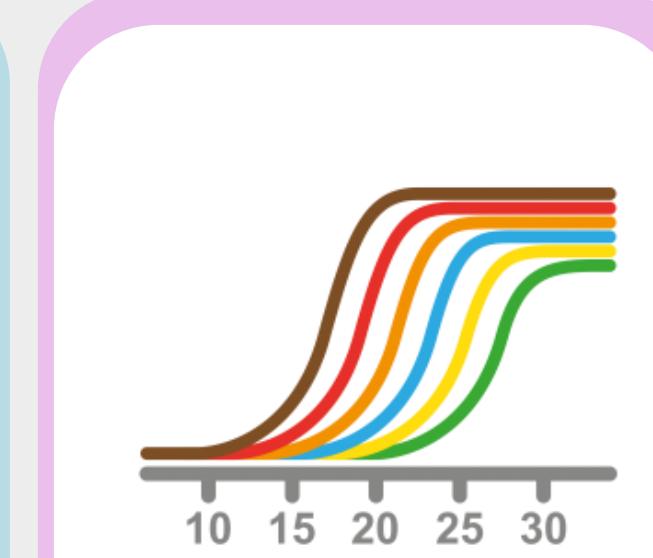
CCRAC / CU



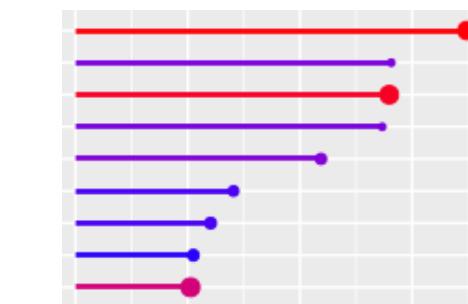
Glycobiological
signature



RT-qPCR

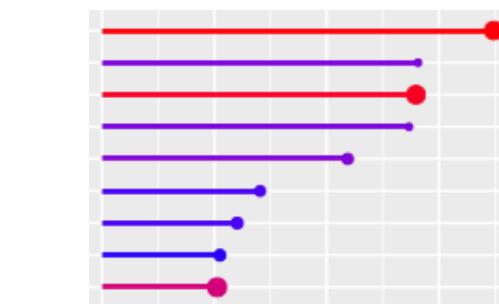


In silico



- General (GSE224758, 37283, 73661, 87473, 92415, 206285)
- qUC (GSE37283)

Patients

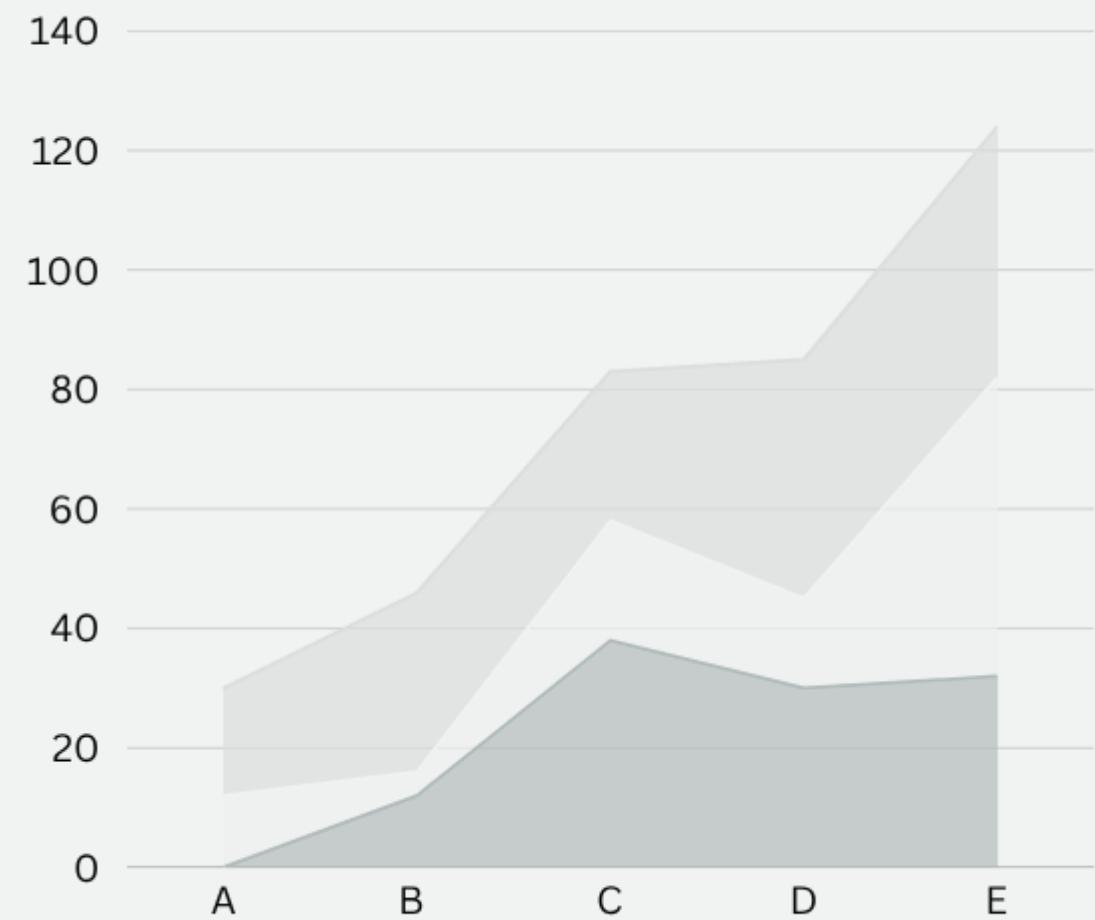


- Pancolitis (GSE47908)
- CU-I (GSE47908)
- CCRAC / pancolitis (GSE3629)
- Pancolitis / CU-I (GSE47908)

In vivo



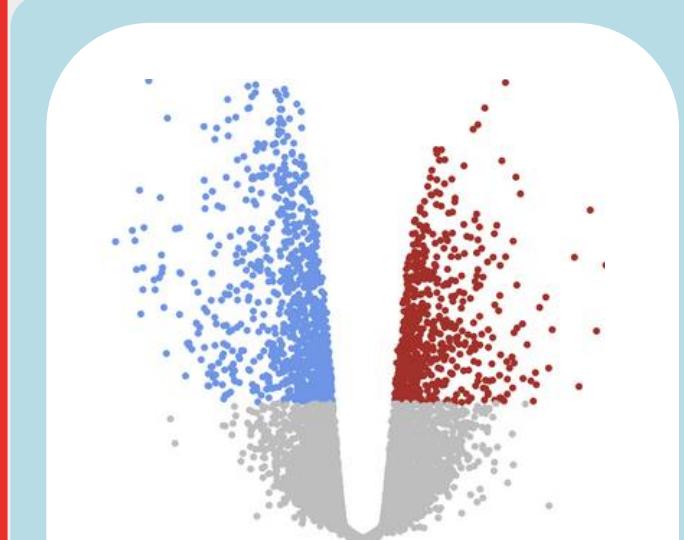
Murine models



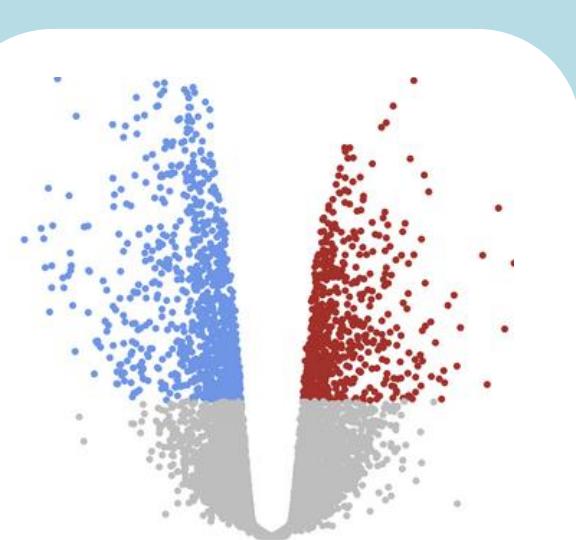
RESULTS

EXPERIMENTAL DESIGN

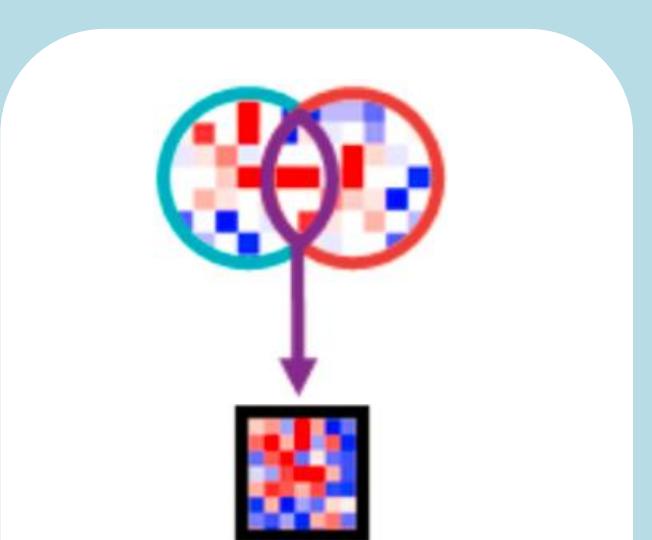
CU / Healthy



Displasia / CU



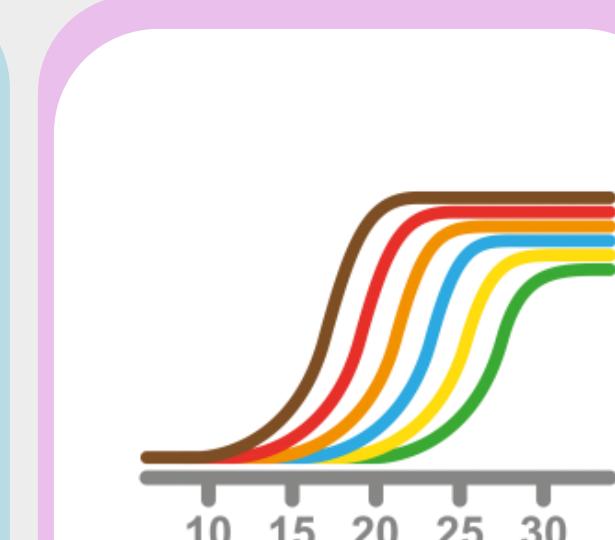
CCRAC / CU



Glycobiological
signature



RT-qPCR

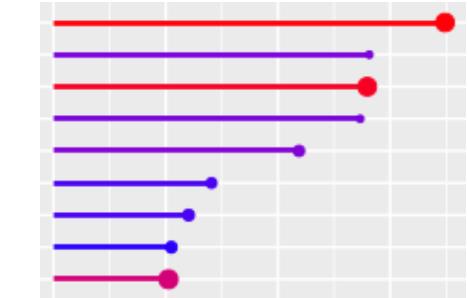


In vivo

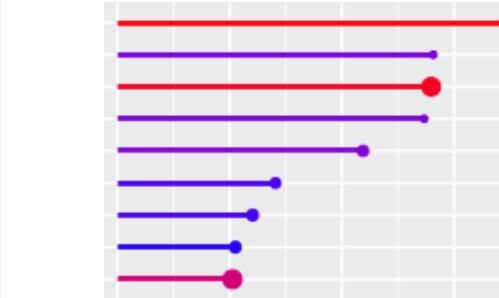
In silico



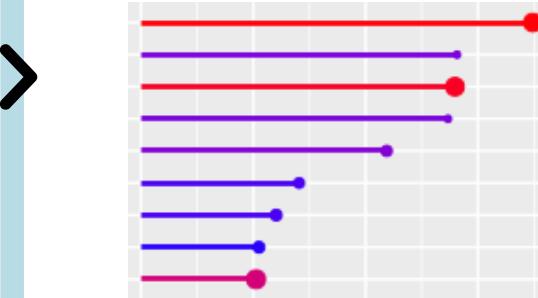
- General (GSE224758, 37283, 73661, 87473, 92415, 206285)
- qUC (GSE37283)



- Pancolitis (GSE47908)
- CU-I (GSE47908)



- CCRAC / pancolitis (GSE3629)
- Pancolitis / CU-I (GSE47908)



- Adenocarcinoma (AOM-DSS) / Inflammation (DSS) (GSE31106)

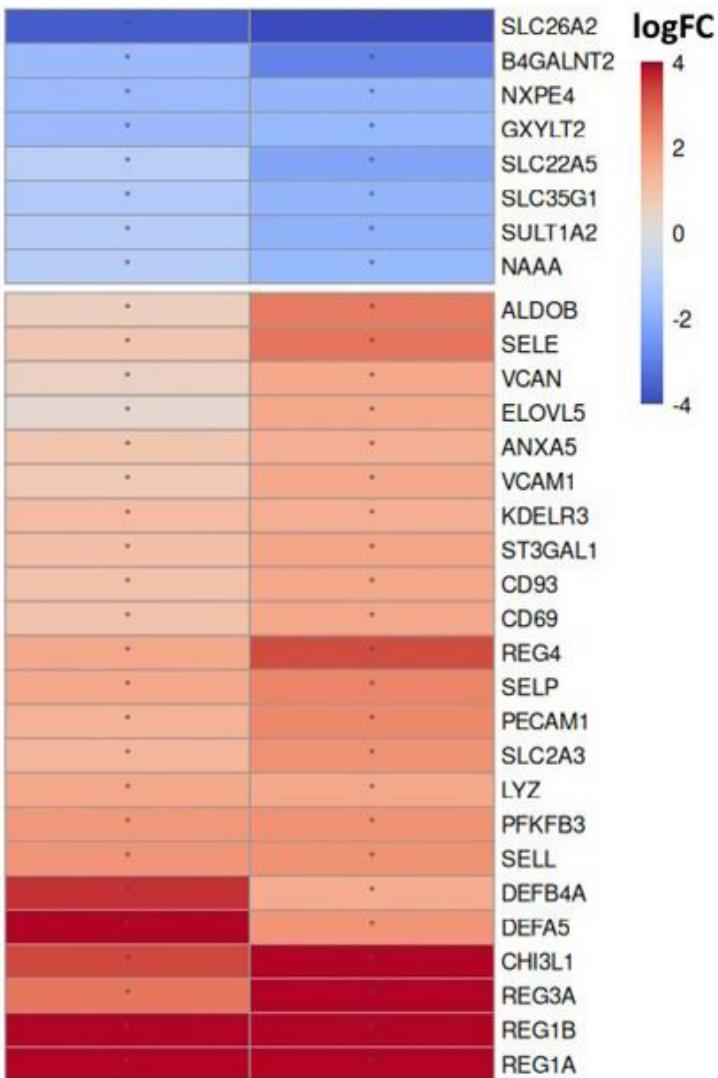


Patients

Murine models

UC / HEALTHY

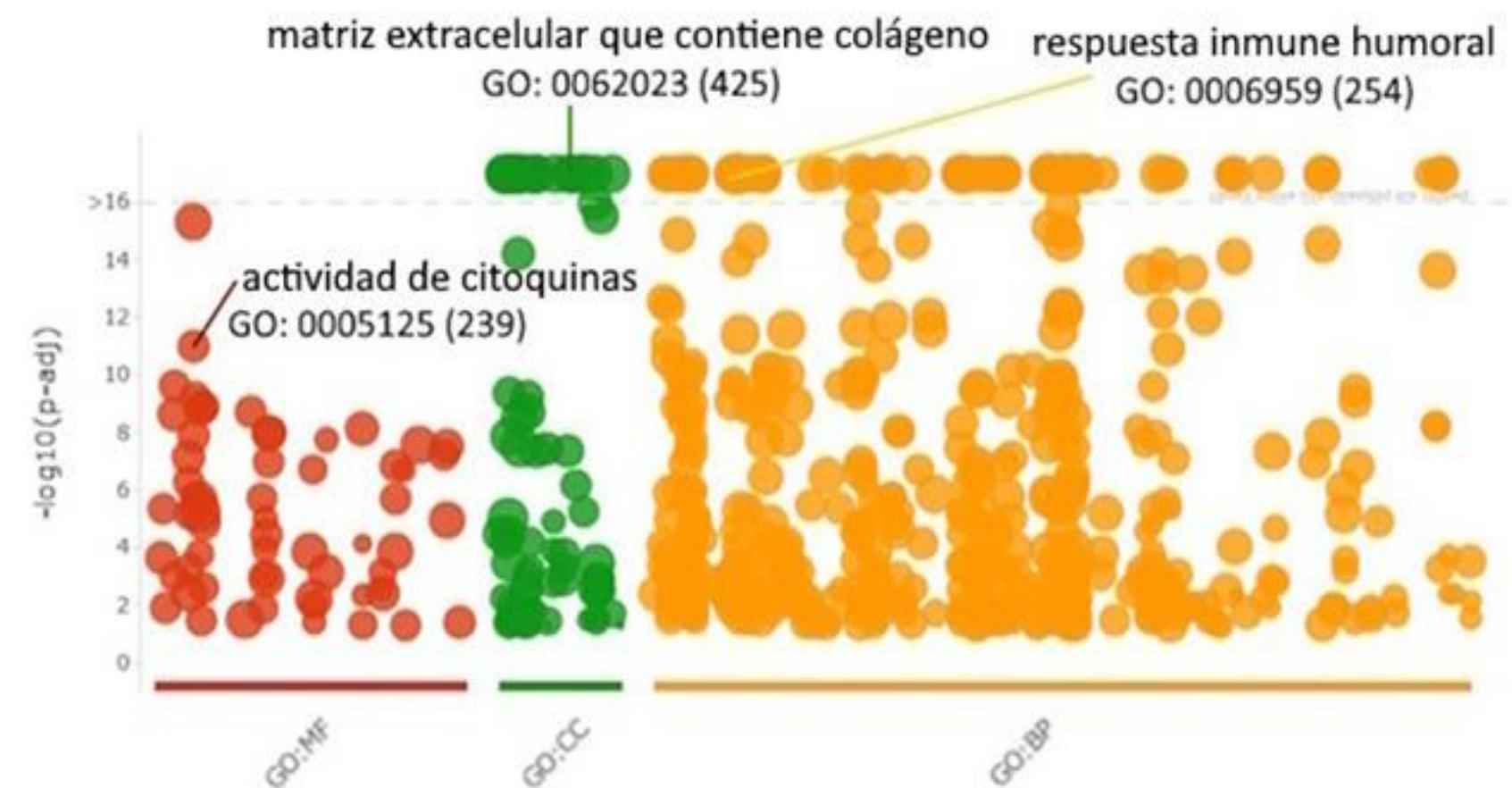
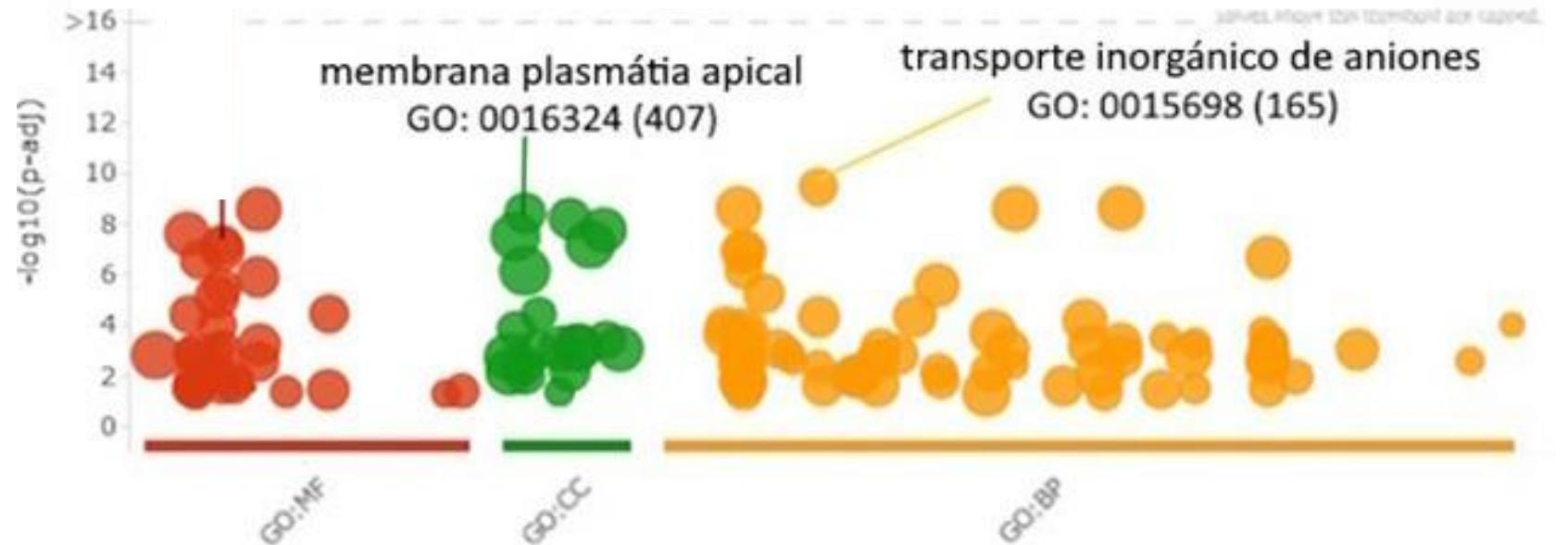
Glycogenes



CU-Izquierdo/Sanos (GSE73661)

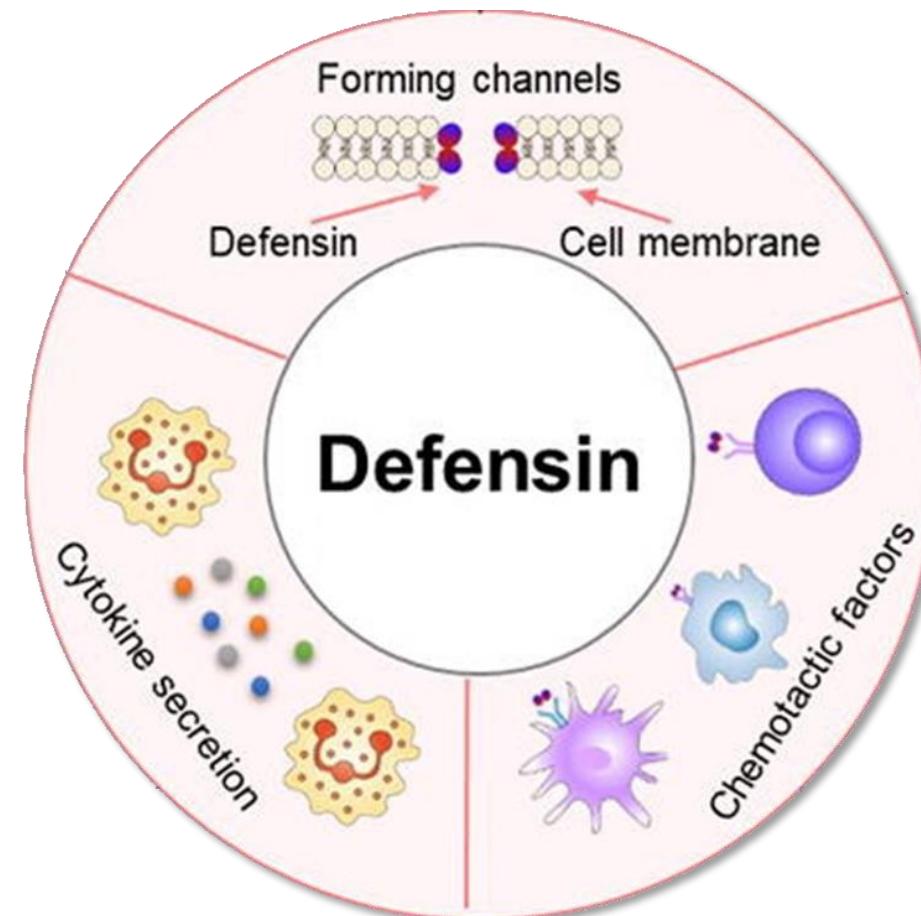
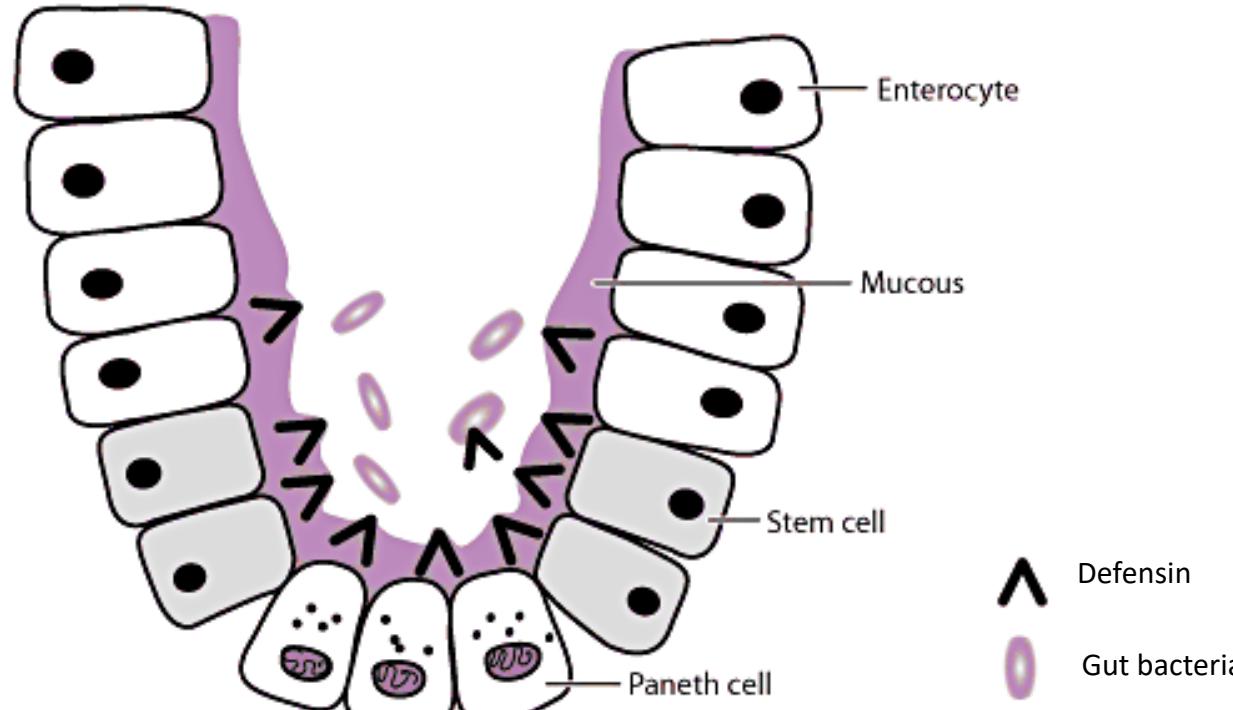
CU/Sanos (GSE73661)

CU-Izquierdo/Sanos (GSE47908)



Results

DEFA5

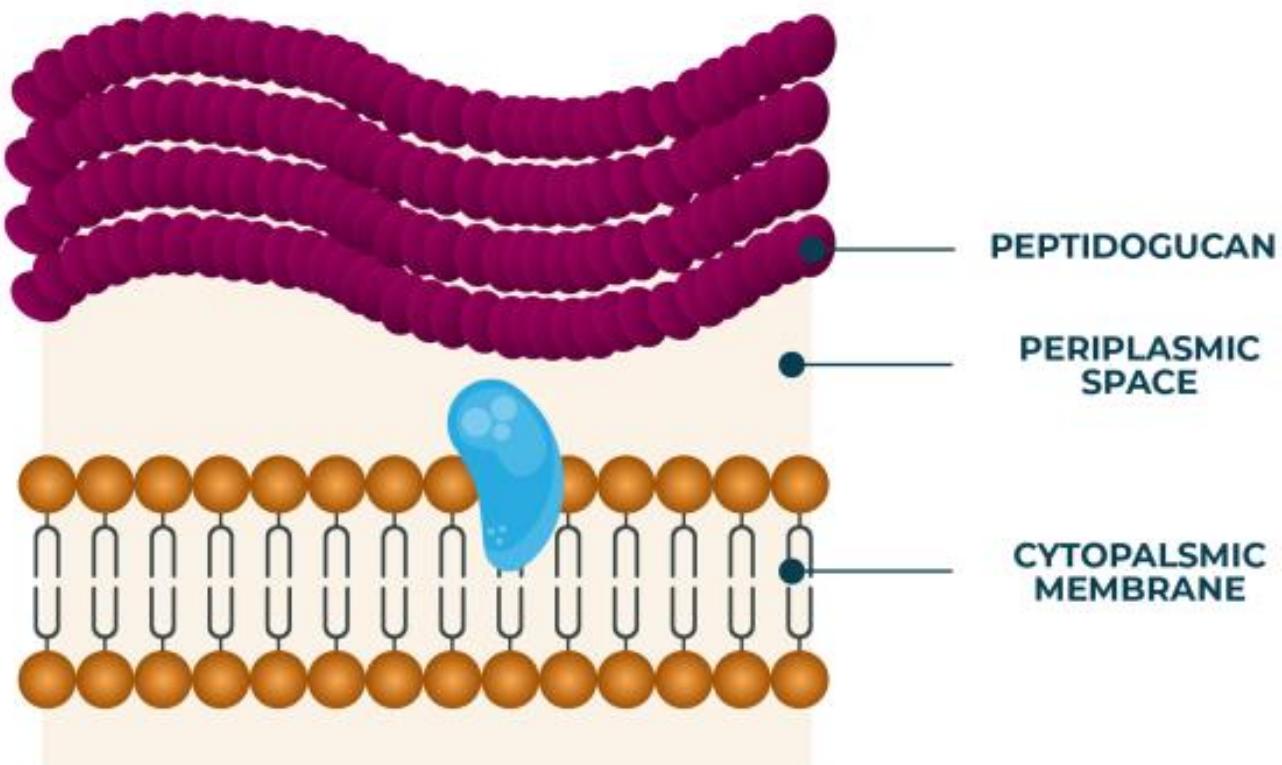
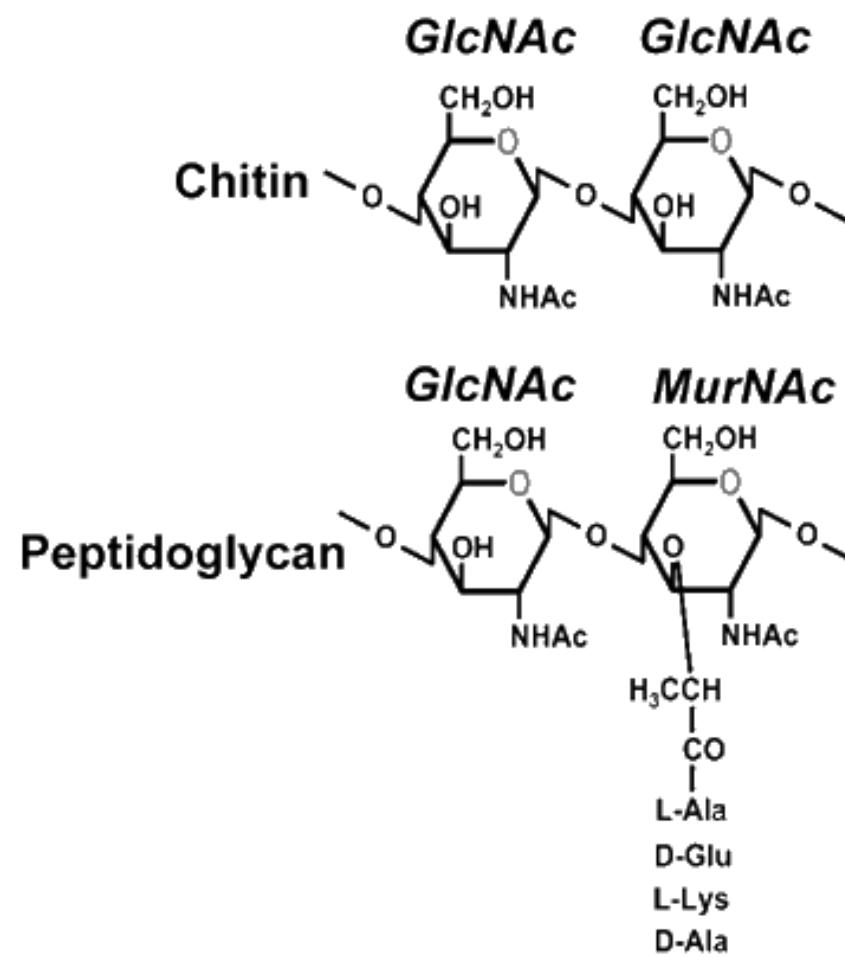


Gao et al (2021). Defensins: The natural peptide antibiotic. Doi: 10.1016/j.addr.2021.114008

- Not expressed in healthy tissue
- ↑ in UC, proposed as a biomarker vs CD



CHI3L1

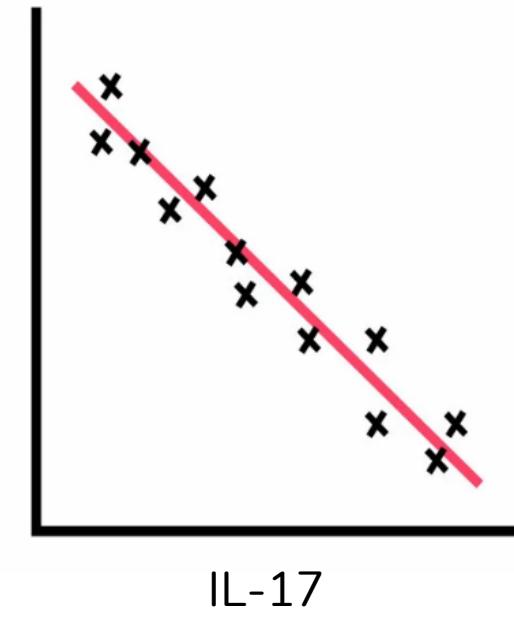
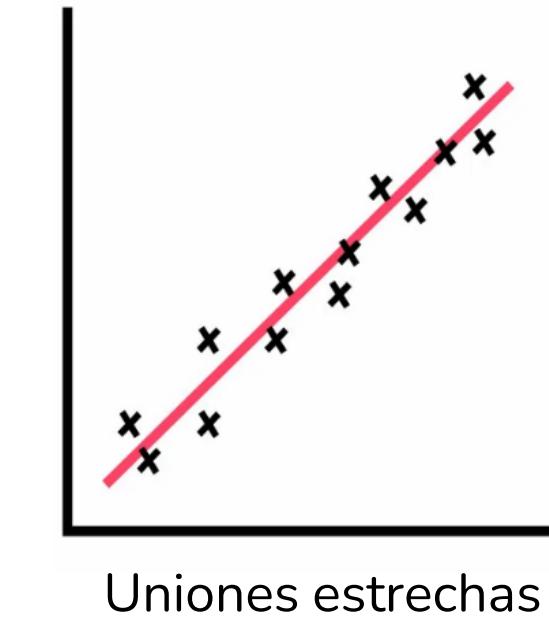
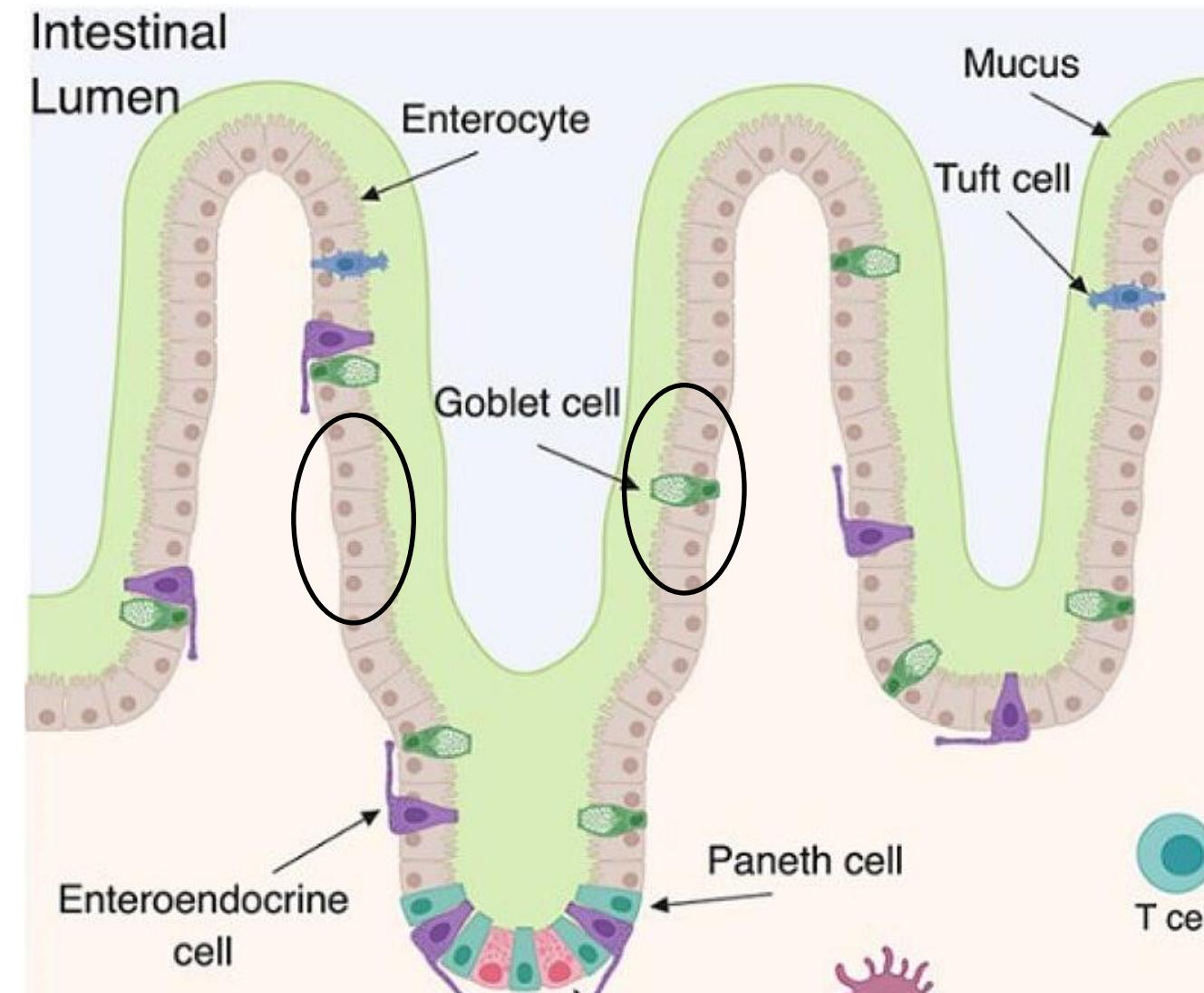
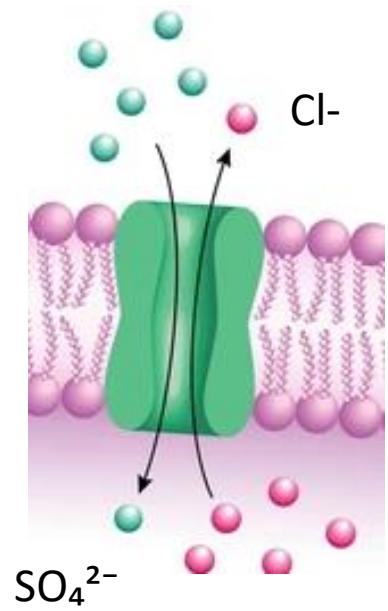


Anchoring
commensal
bacteria



- ↑ in serum (CU)
- Expression associated with immune cells
- Chronic inflammation: Wnt/β-catenin

SLC26A2



- ↓ on active CU and DSS models
- Key in mucin sulfation, reduced in IBD

Results

REMISSION STATUS

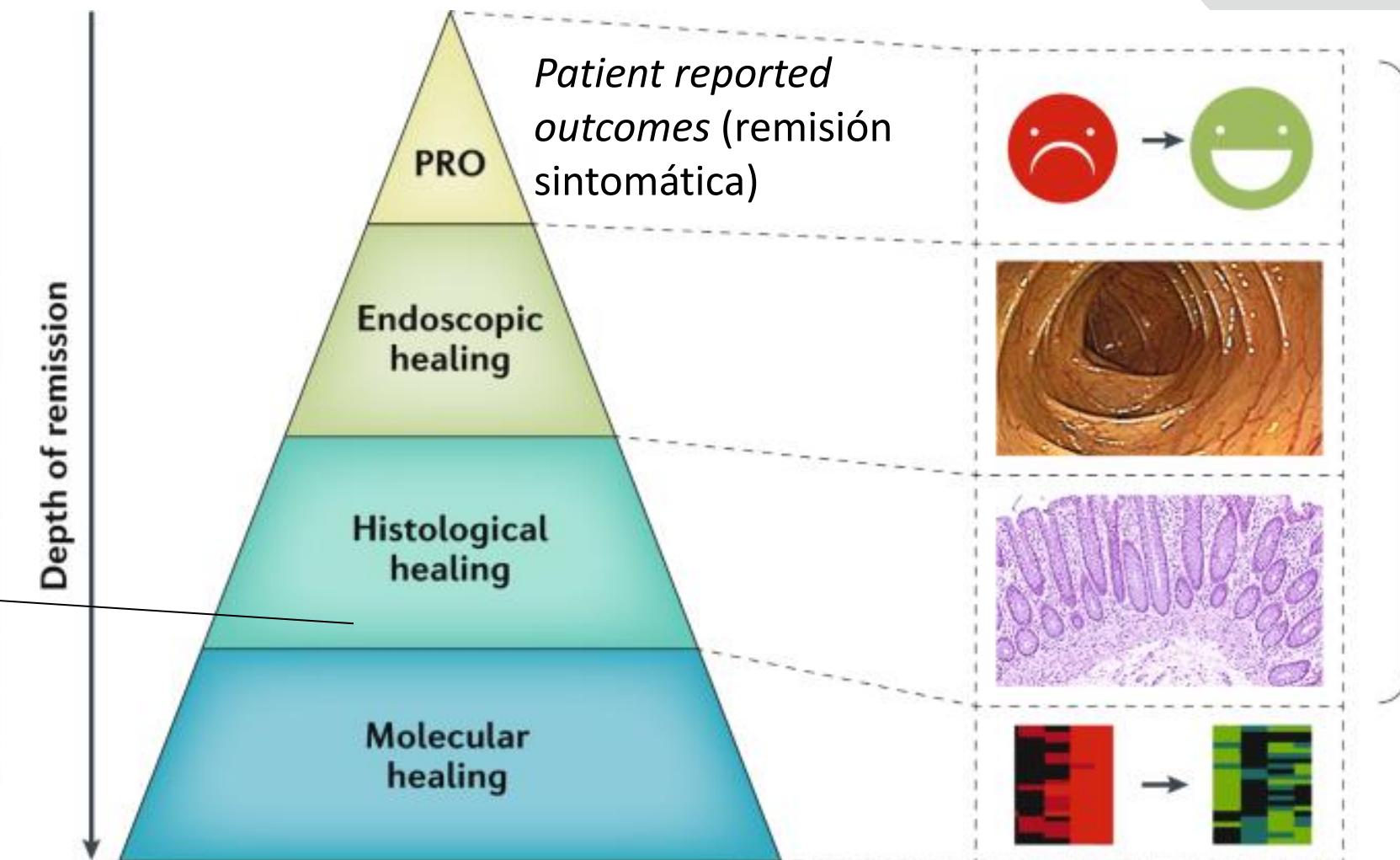
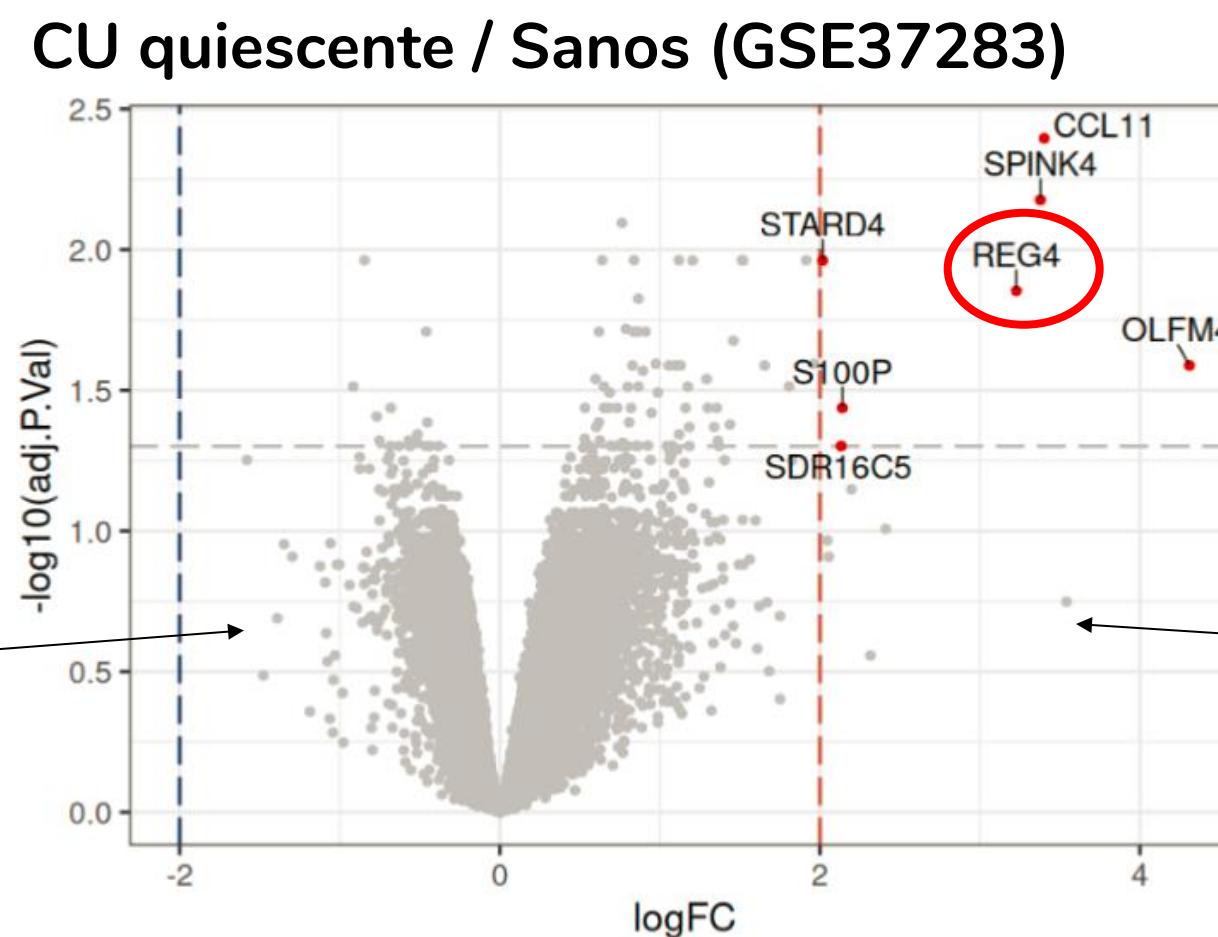
In histological remission there are glycobiological alterations



Moderate UC



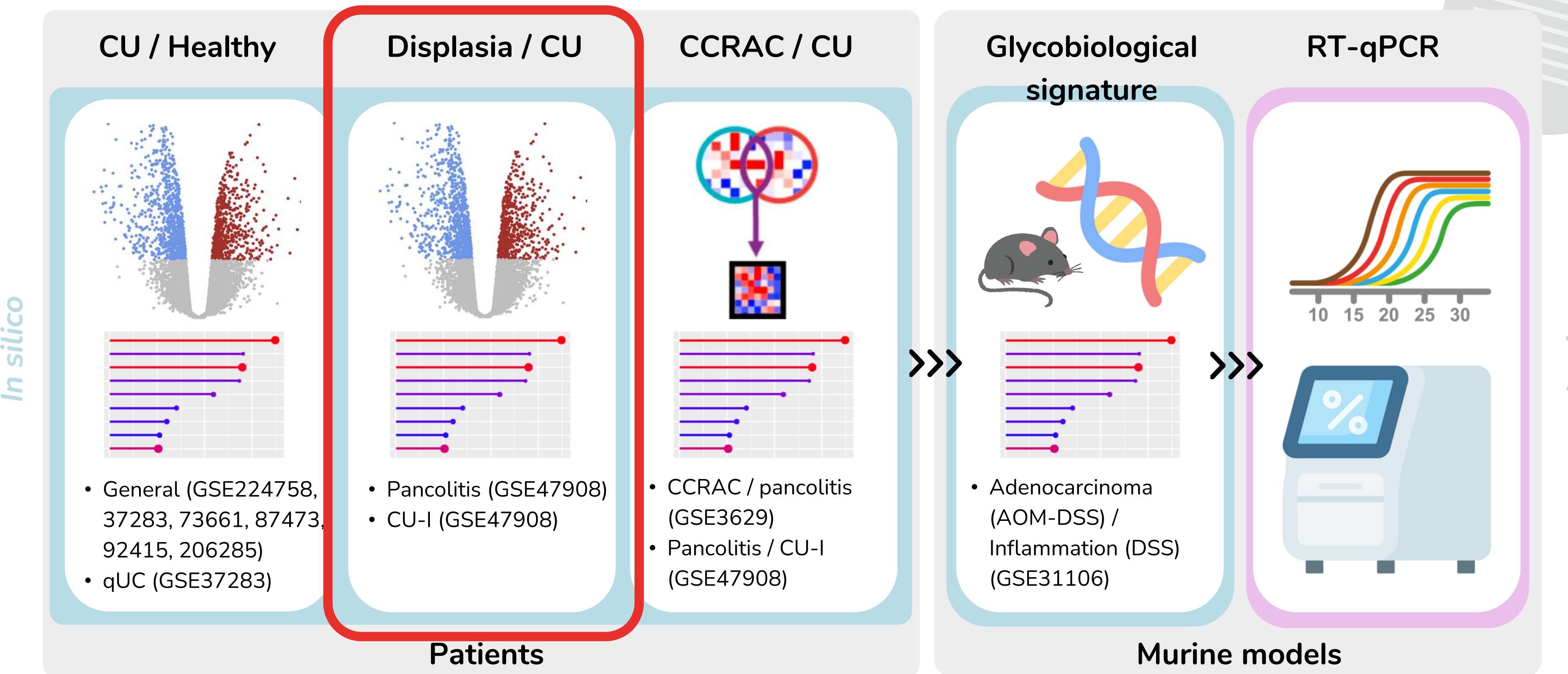
Endoscopic remission



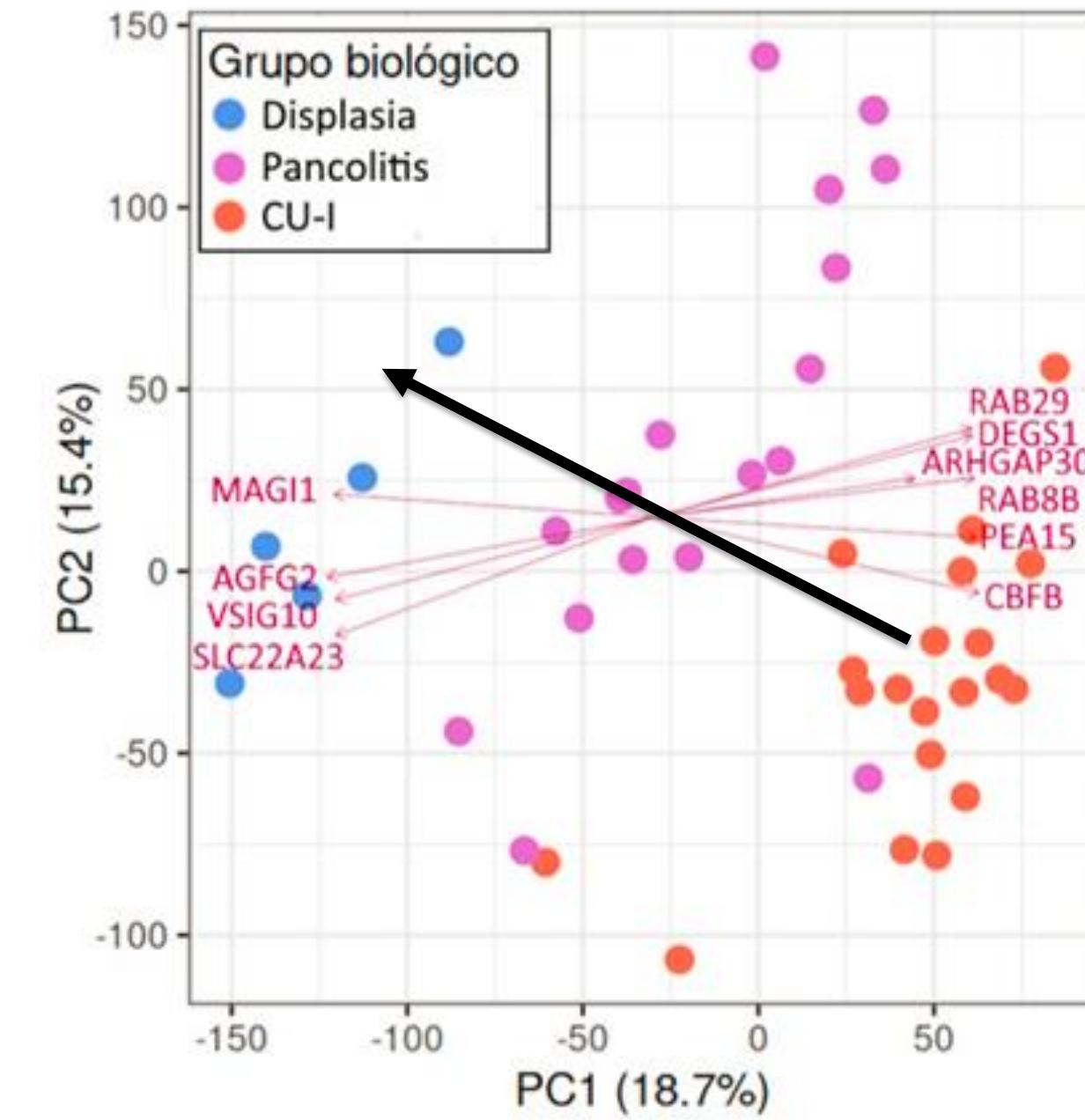
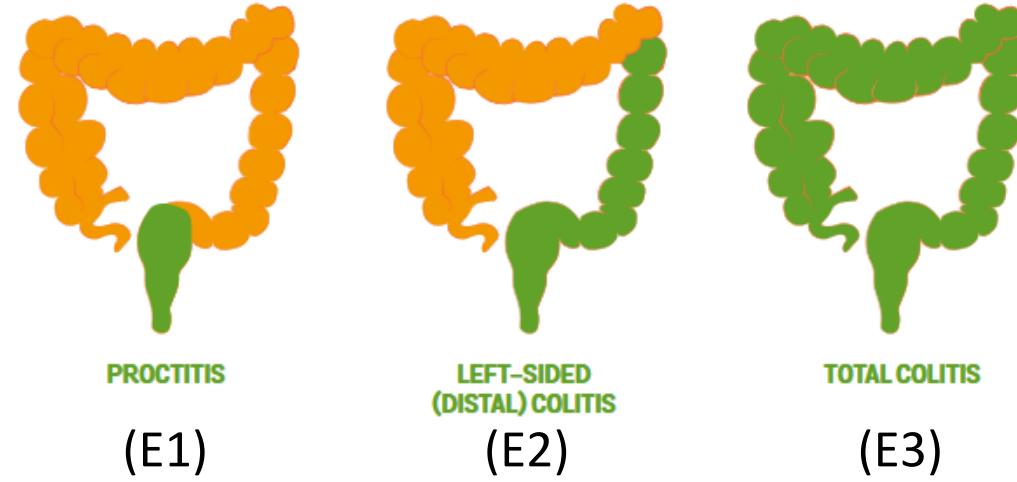
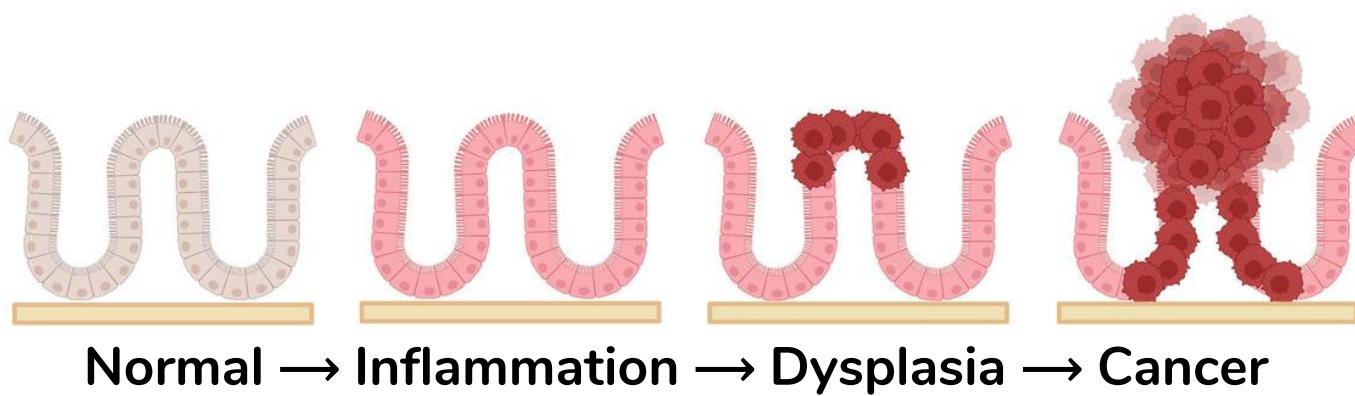
Dalal et al (2021), Two Strikes but Not Out: Deep Remission of Ulcerative Colitis with Ustekinumab After Primary Non-response to Infliximab and Vedolizumab. Doi: 10.1007/s10620-021-06852-3

Danese et al (2020). Evolving therapeutic goals in ulcerative colitis: towards disease clearance. Doi: doi.org/10.1038/s41575-019-0211-1

EXPERIMENTAL DESIGN



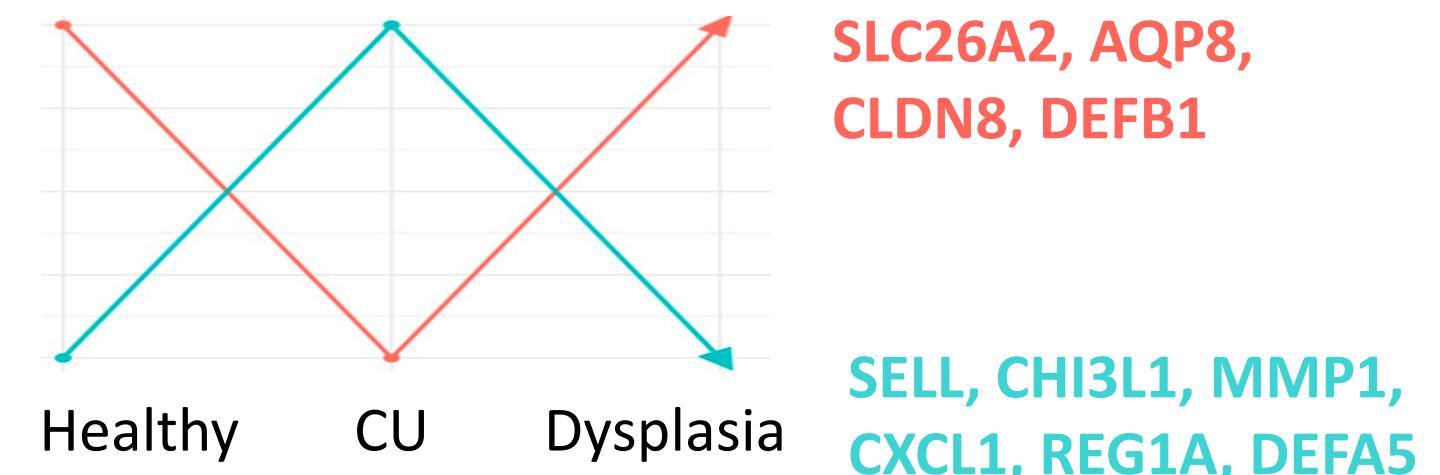
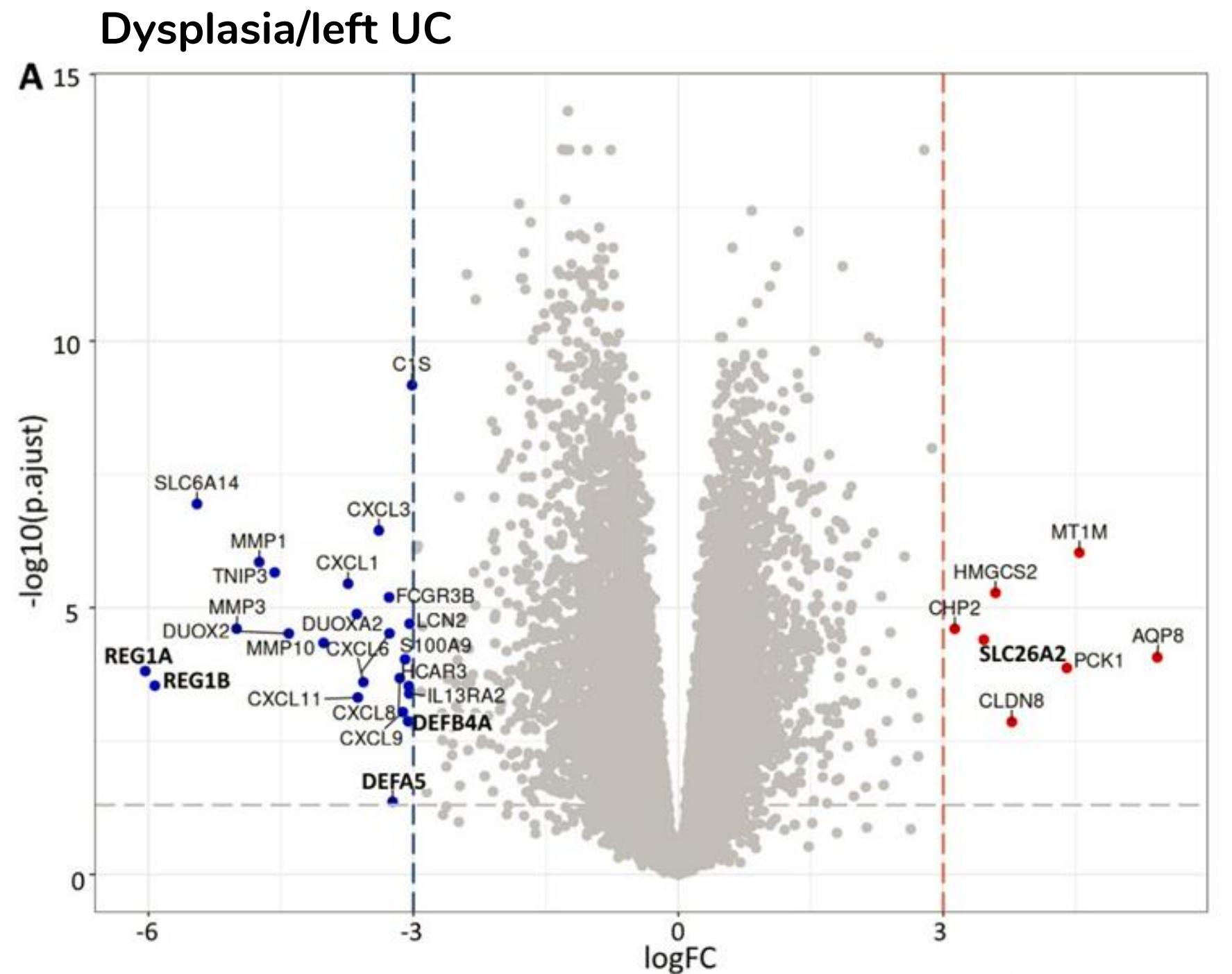
DYSPLASIA / UC



Pancolitis (E3) is molecularly closer to dysplasia than left UC (E2)

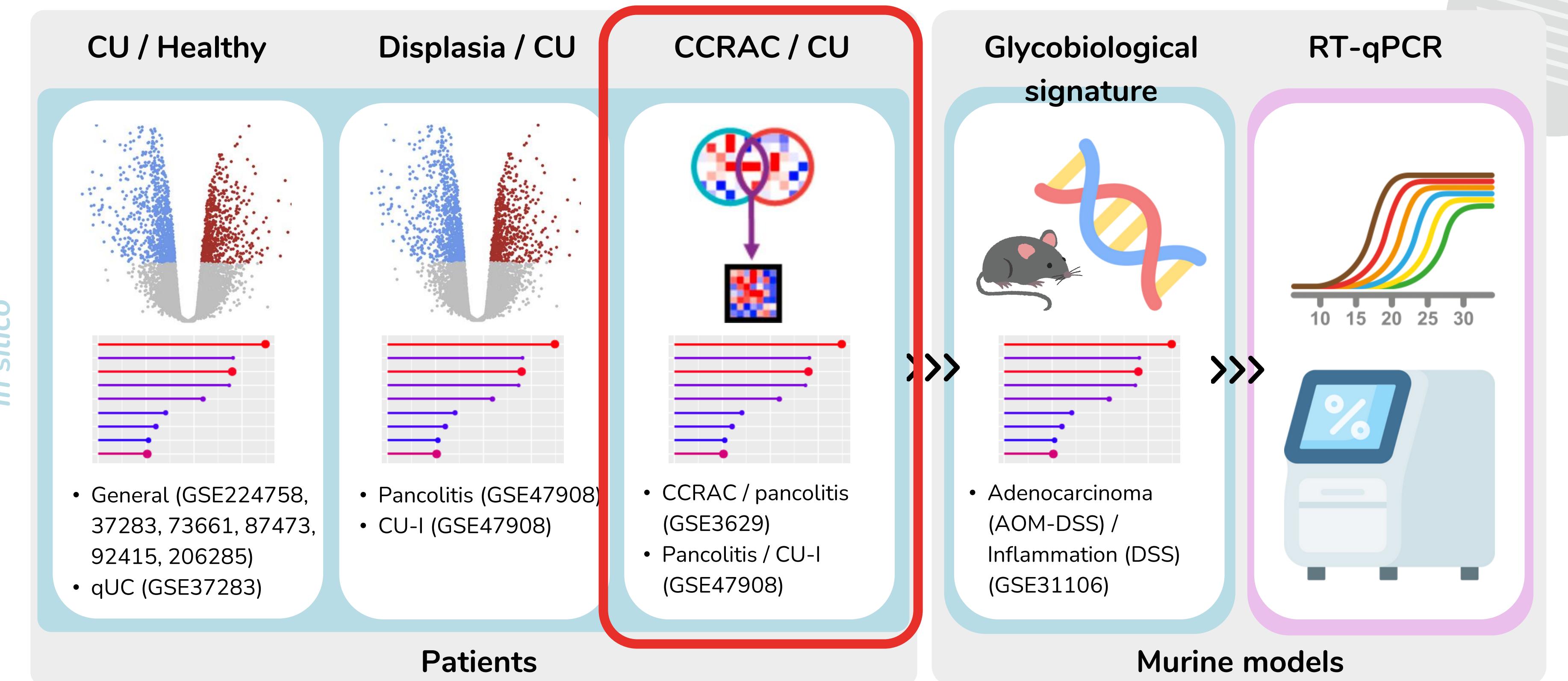
DYSPLASIA / LEFT UC

Glycogene dysregulation patterns are opposite from healthy to inflamed and then dysplastic tissue



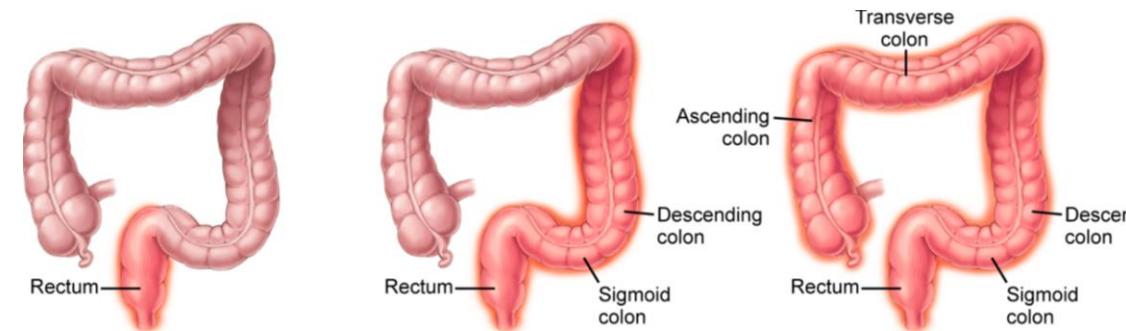
Results

EXPERIMENTAL DESIGN

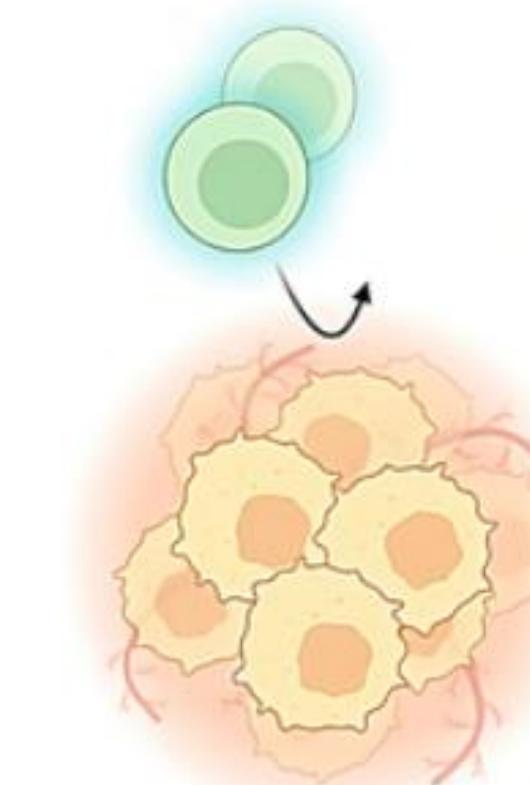
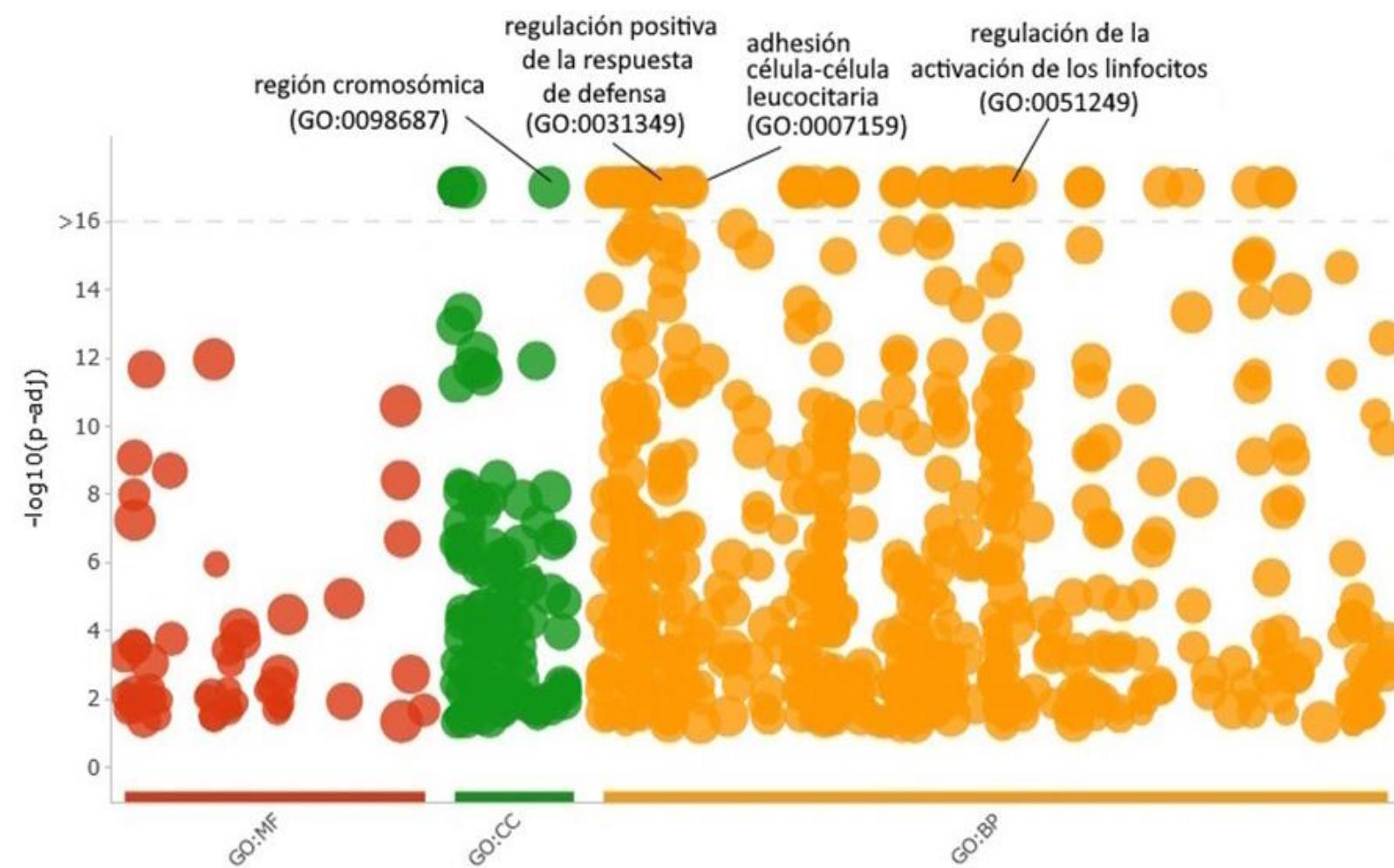


UC AND CACRC / LEFT UC

Left UC (E2) → Pancolitis (E3) → UC+ CACRC

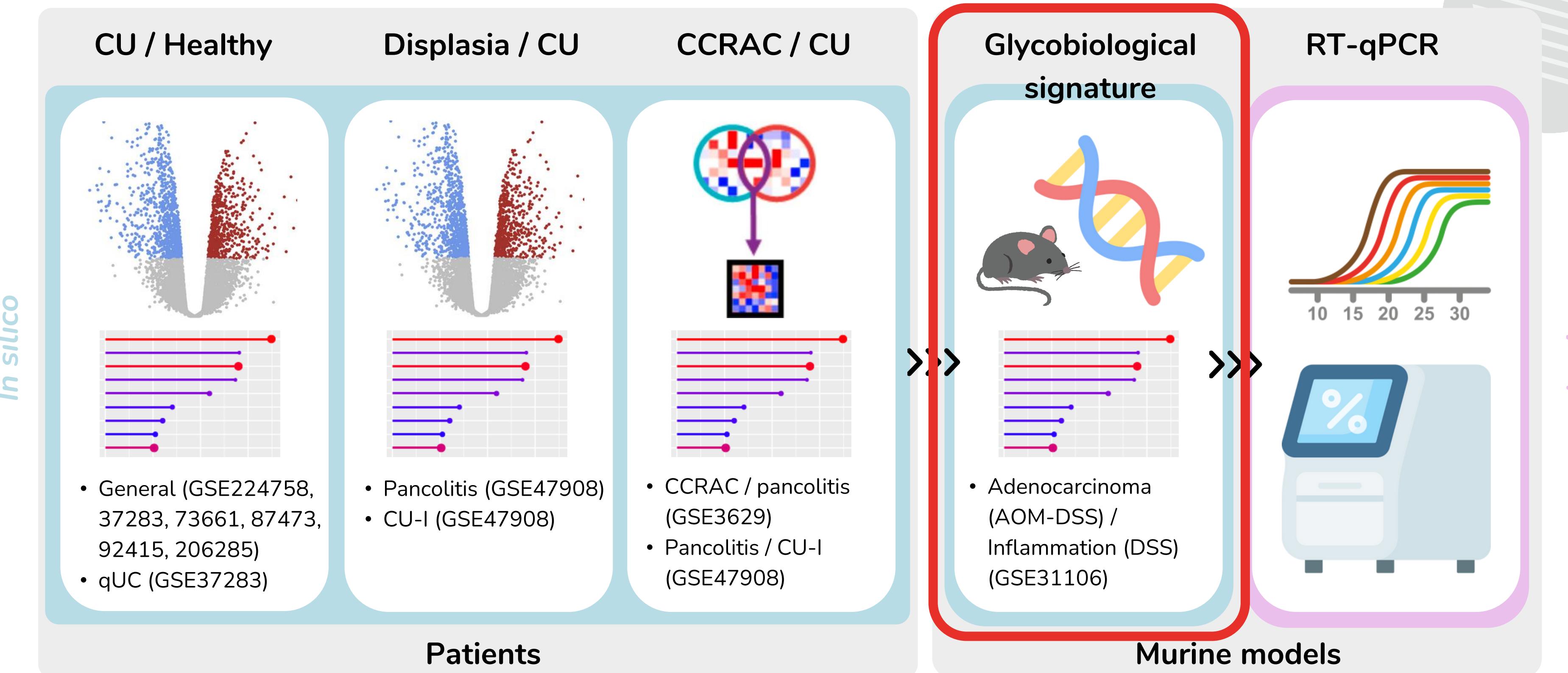


Cumulative Inflammatory Burden (CIM)
(Carga inflamatoria acumulativa)

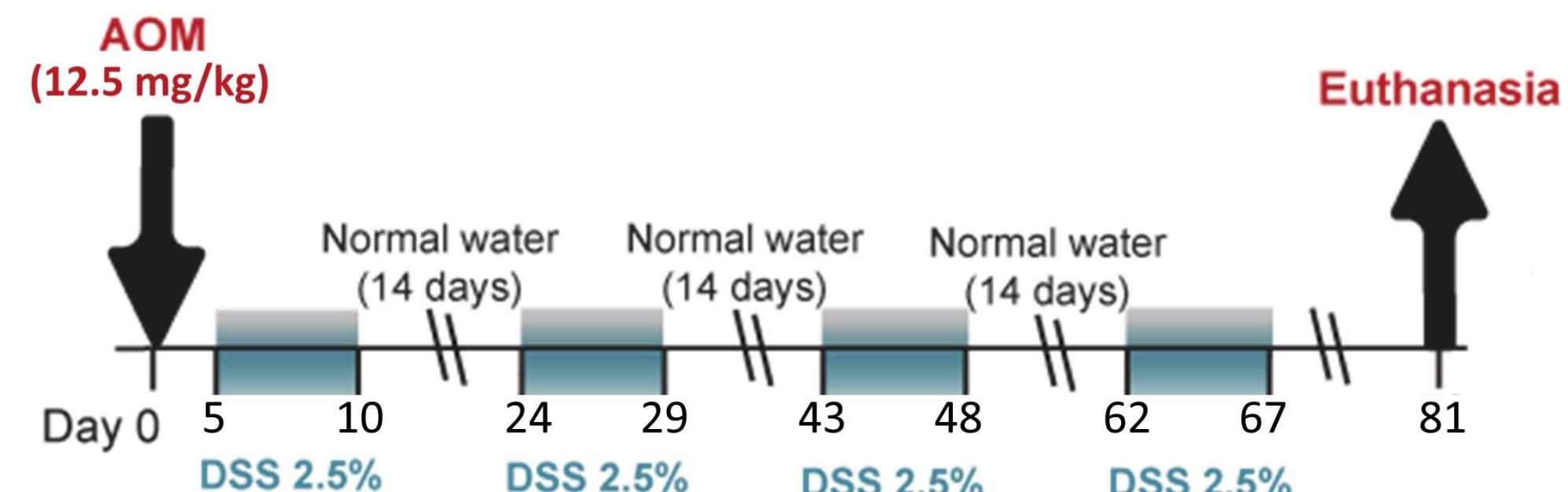
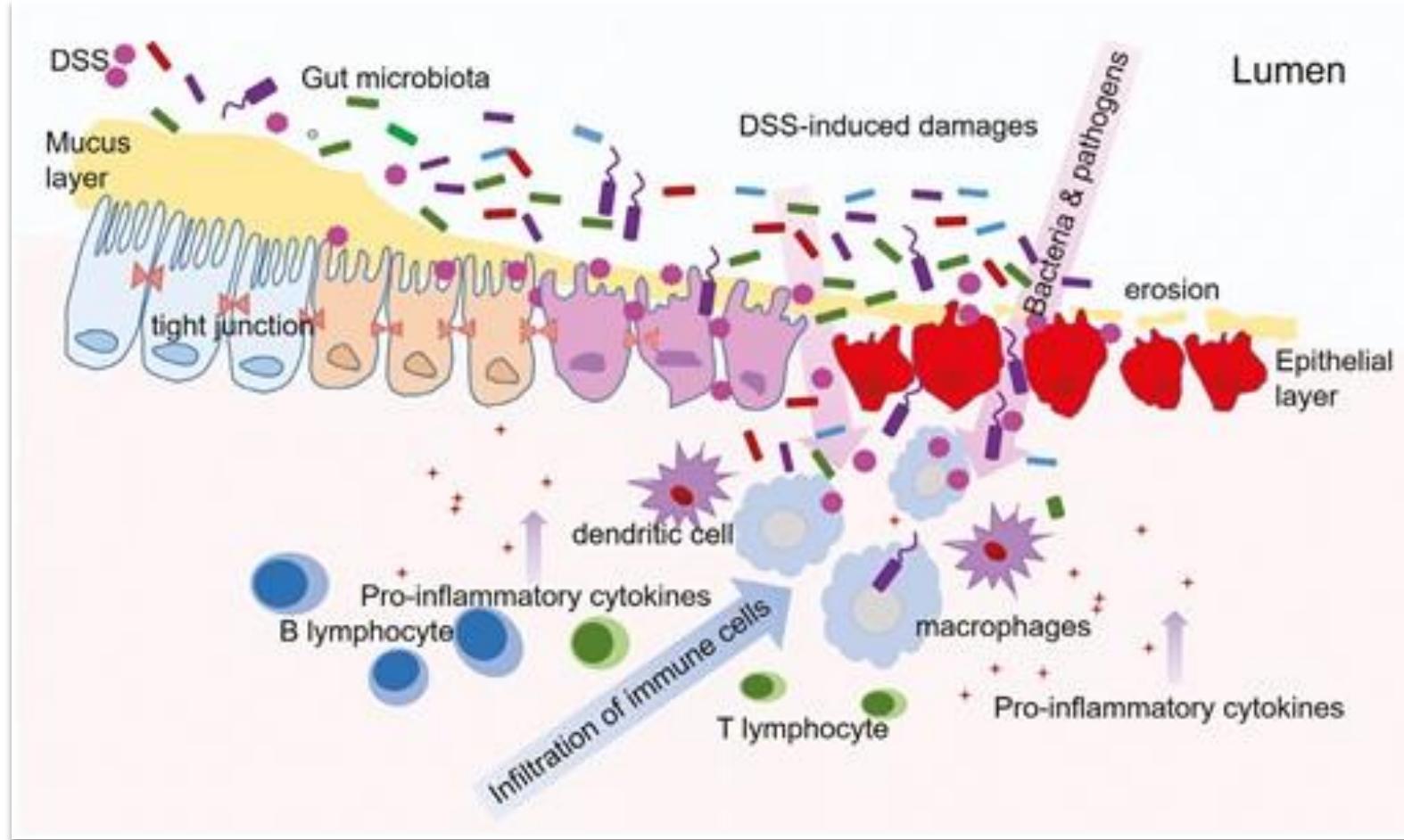


Results

EXPERIMENTAL DESIGN



MURINE MODEL OF CACRC INDUCED BY AOM-DSS

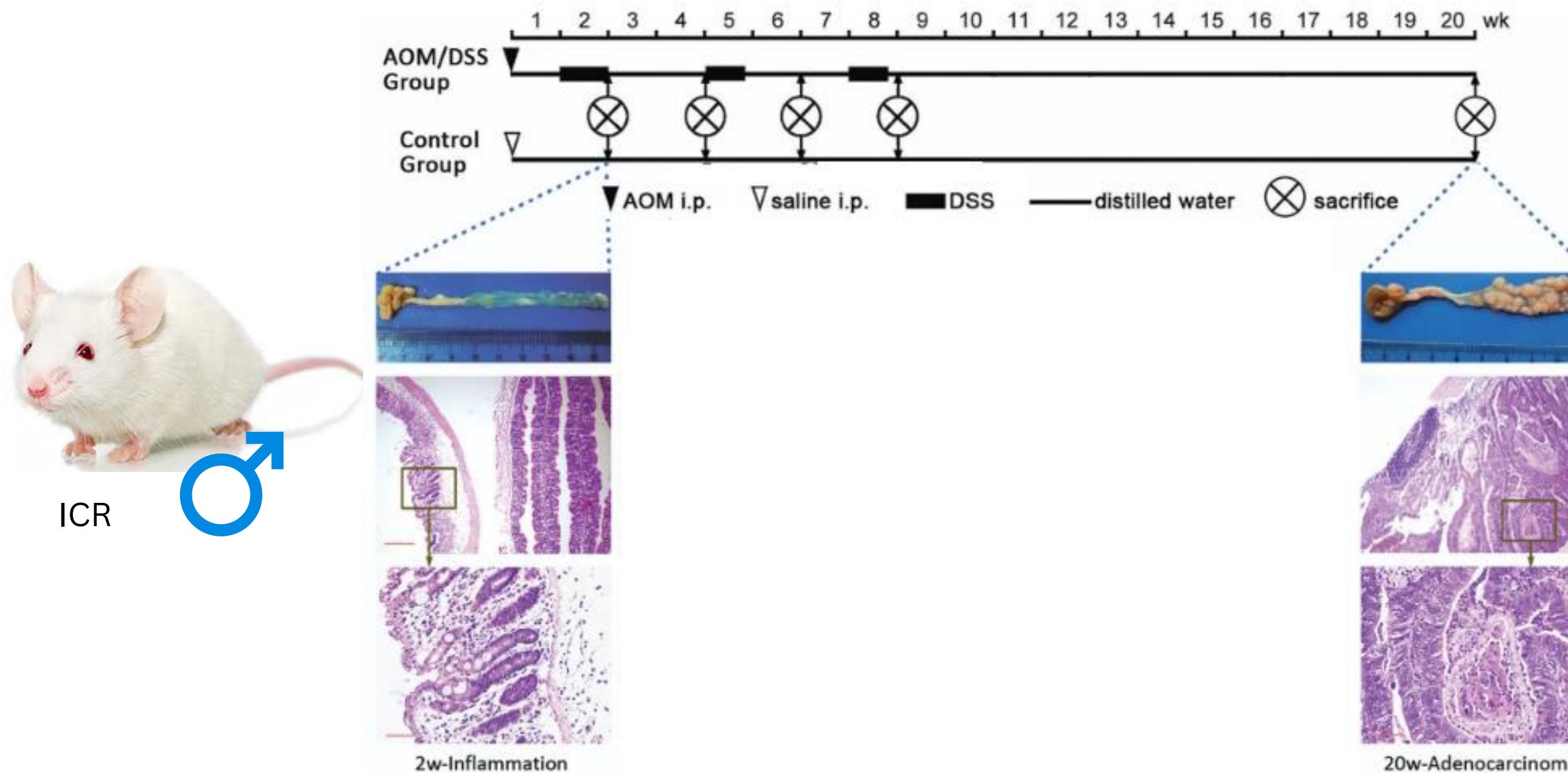


Chunhua et al. (2024). Unveiling Colitis: A Journey through the Dextran Sodium Sulfate-induced Model, Inflammatory Bowel Diseases. Doi: 10.1093/ibd/izad312

Results

ADENOCARCINOMA VS INFLAMED

In transcriptomics databases, corresponding to the AOM-DSS model

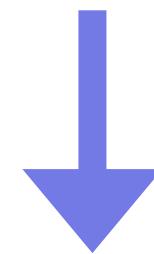
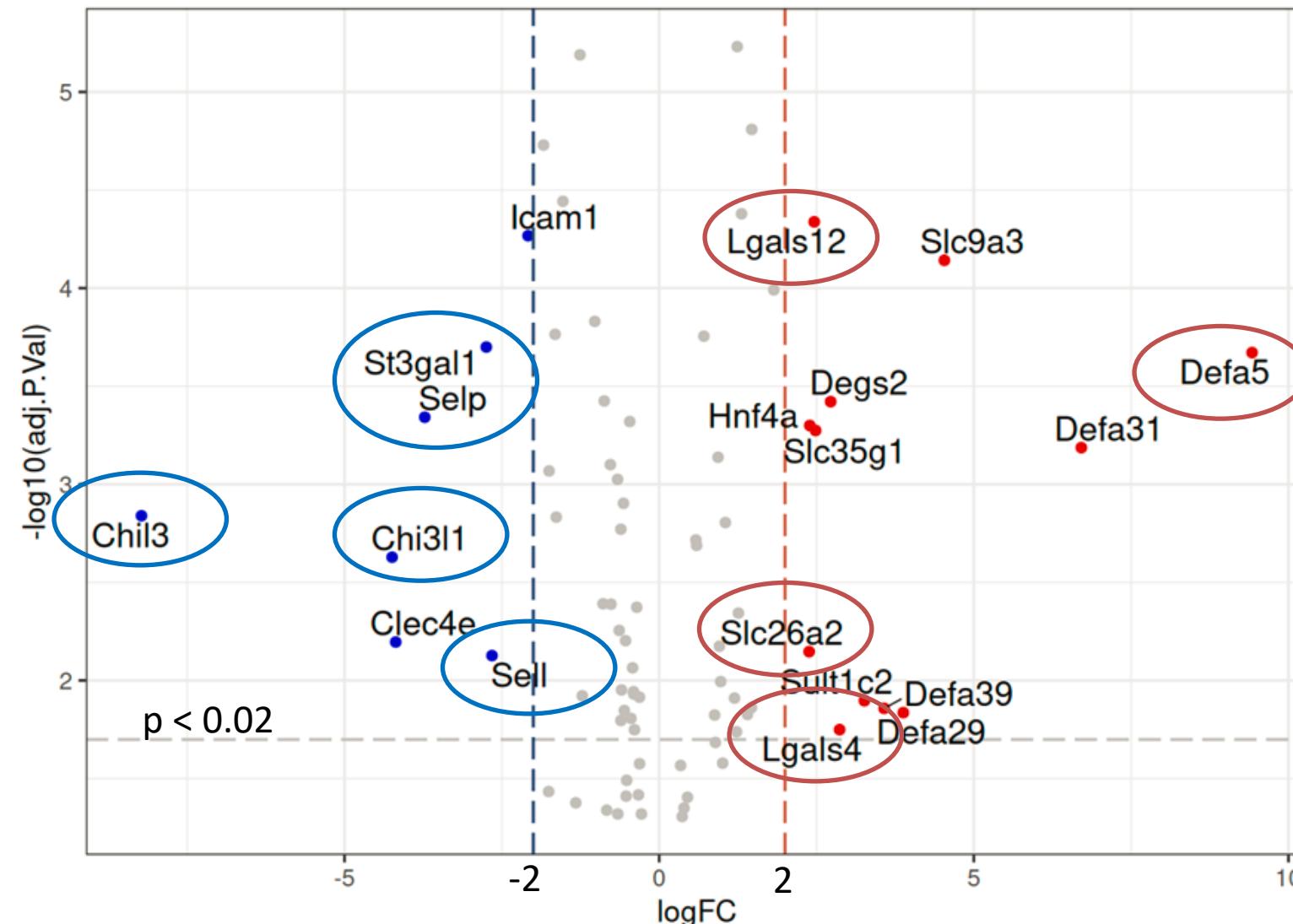


Tang, A., et al (2012). Dynamic activation of the key pathways: linking colitis to colorectal cancer in a mouse model.
Doi: 10.1093/carcin/bgs183

Results

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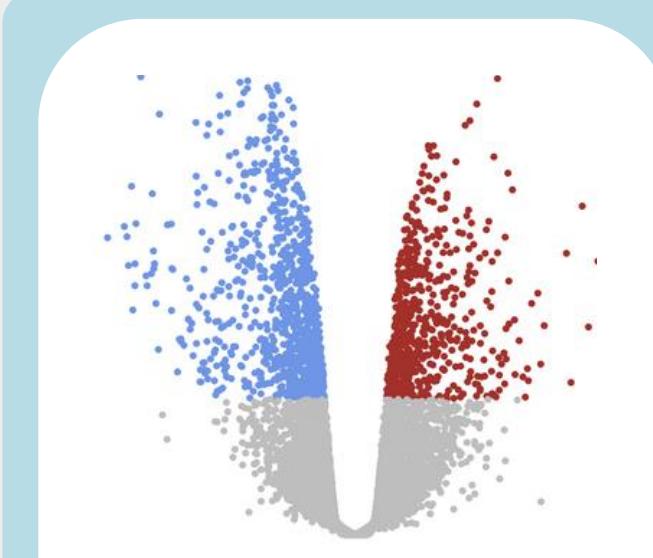


Ratón	Ortólogo humano	Nombre del gen
<i>Defa5</i>	DEFA5	Defensina 5
<i>Lgals4</i>	LGALS4	Galectina 4
<i>Lgals12</i>	LGALS12	Galectina 12
<i>Slc26a2</i>	SLC26A2	Miembro 2 de la familia de portadores de solutos 26
<i>Icam1</i>	ICAM1	Molécula de adhesión intercelular 2
<i>Sell</i>	SELL	Selectina L
<i>Selp</i>	SELP	Selectina P
<i>St3gal1</i>	ST3GAL1	ST3 Beta-galactósido alfa-2,3-sialiltransferasa 1
<i>Chi3l1</i>	CHI3L1	Proteína 1 similar a la quitinasa 3
<i>Chil3</i>	CHIA	Quitinasa ácida

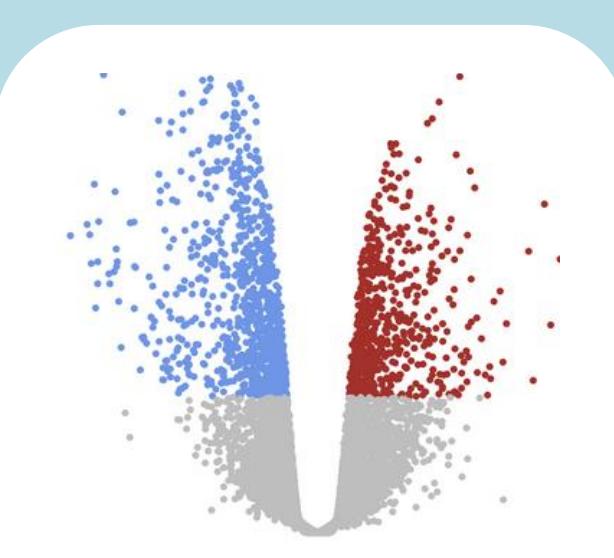
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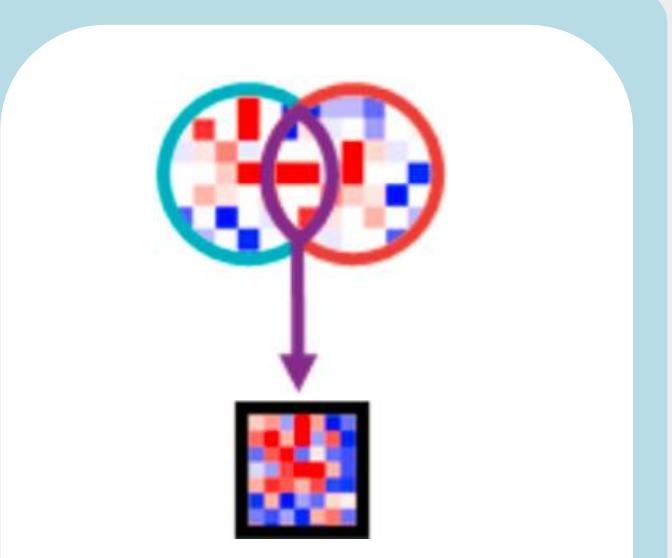
CU / Healthy



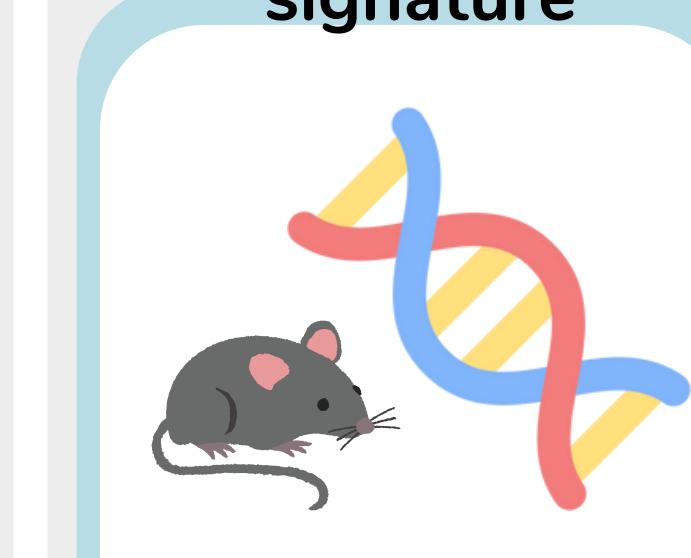
Displasia / CU



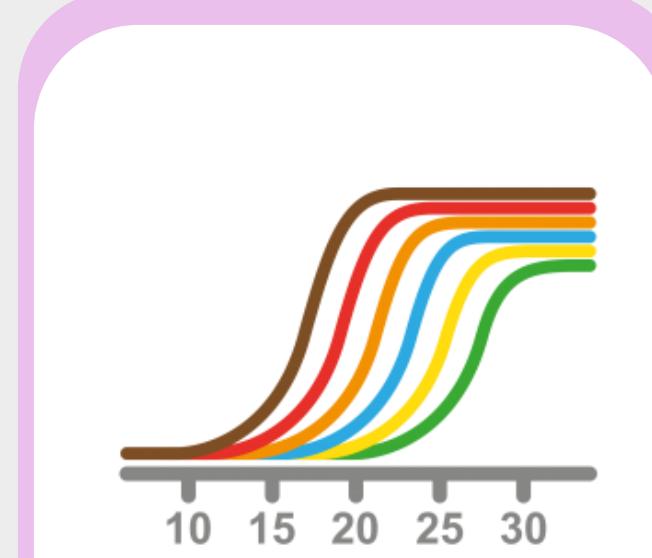
CCRAC / CU



Glycobiological
signature



RT-qPCR



In silico



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- qUC (GSE37283)

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- Pancolitis (GSE47908)
- CU-I (GSE47908)

- CCRAC / pancolitis (GSE3629)
- Pancolitis / CU-I (GSE47908)

- Adenocarcinoma (AOM-DSS) / Inflammation (DSS) (GSE31106)

In vivo

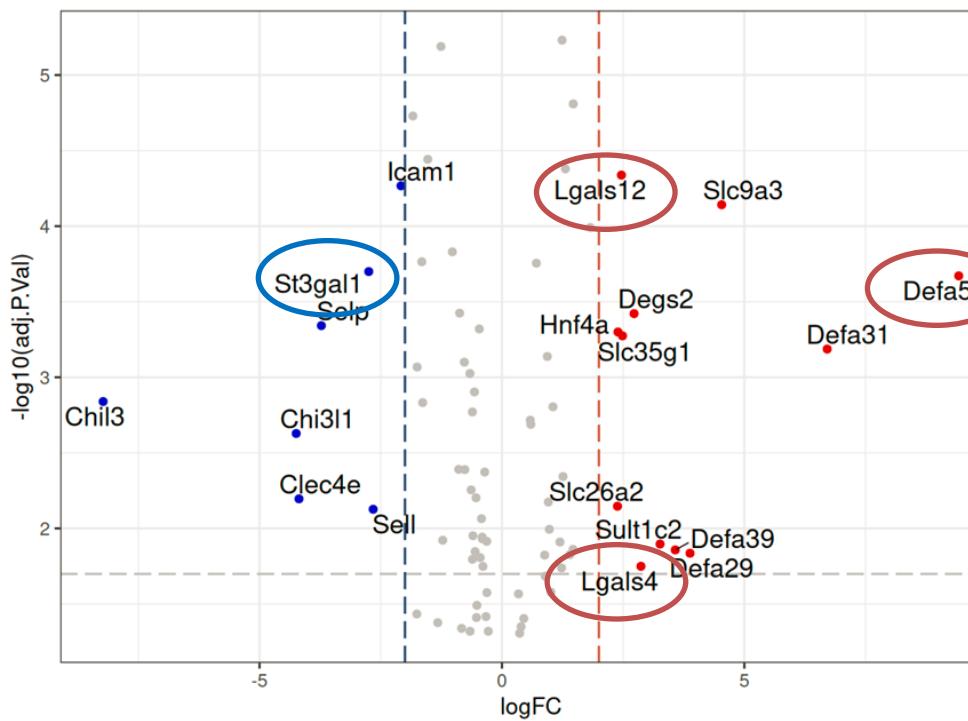
Murine models

QUANTITATIVE RT-PCR



C57BL/6

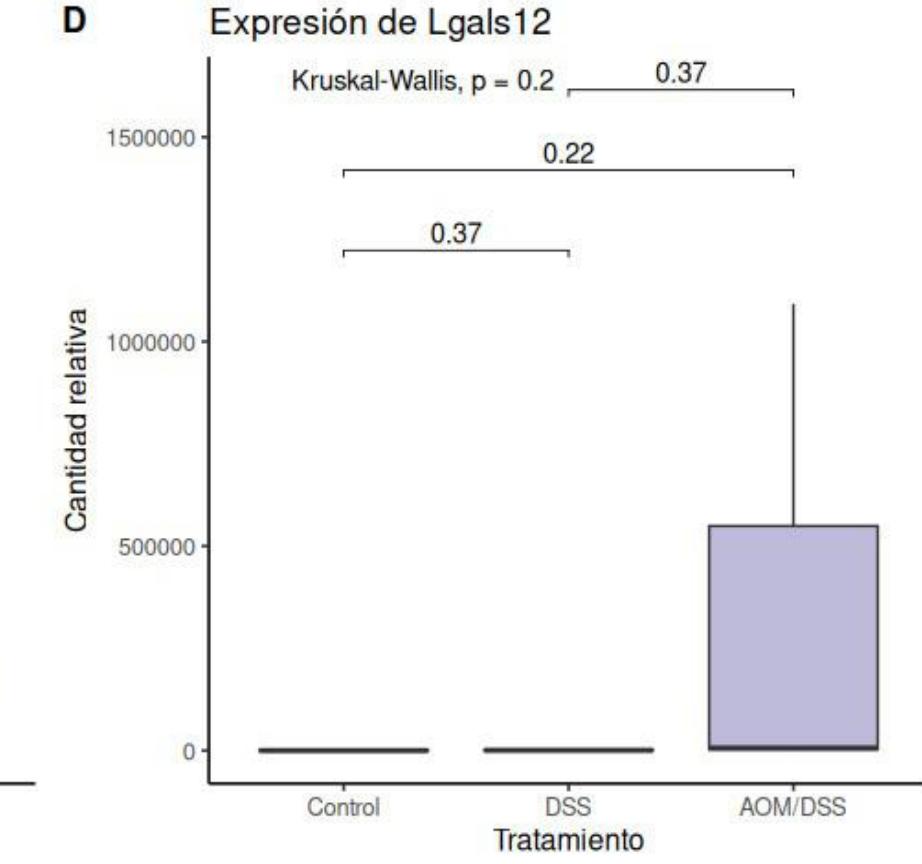
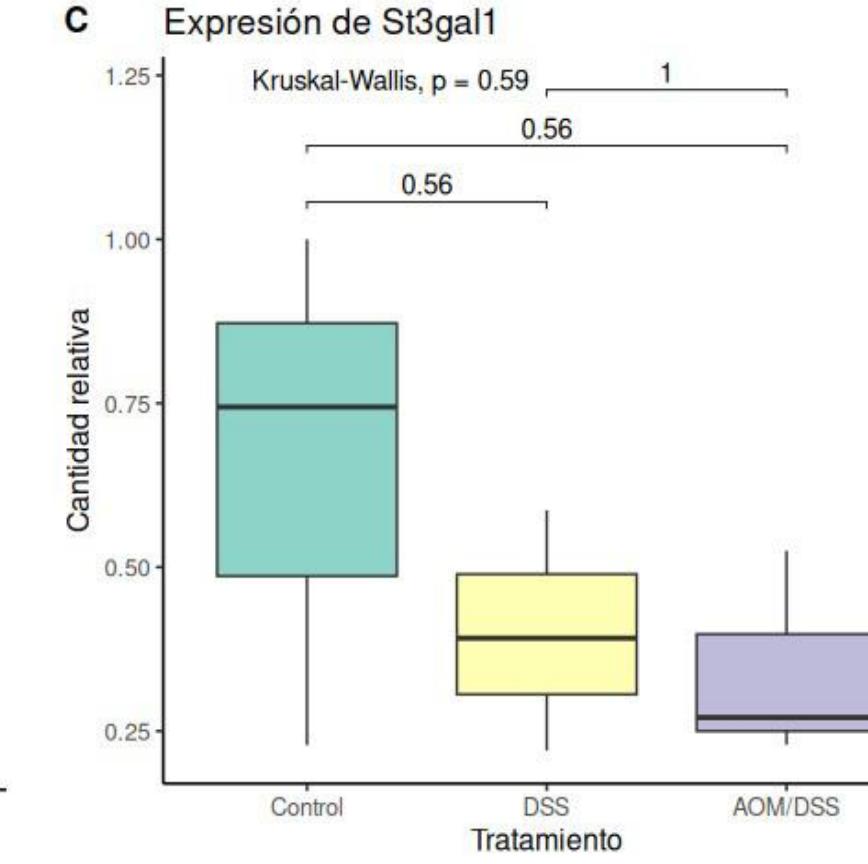
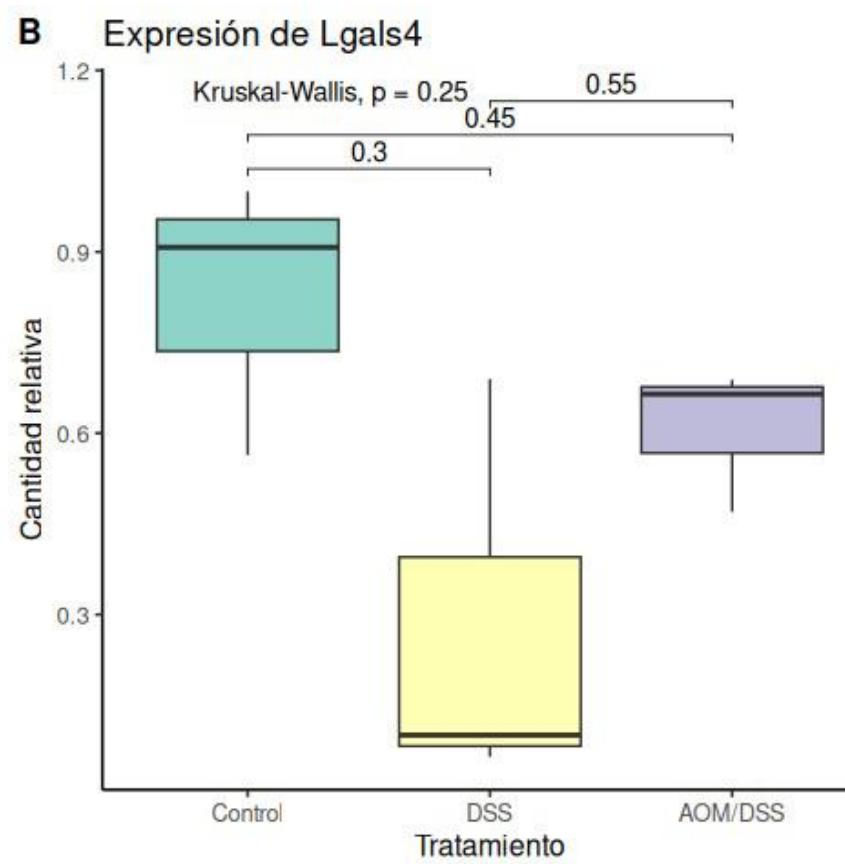
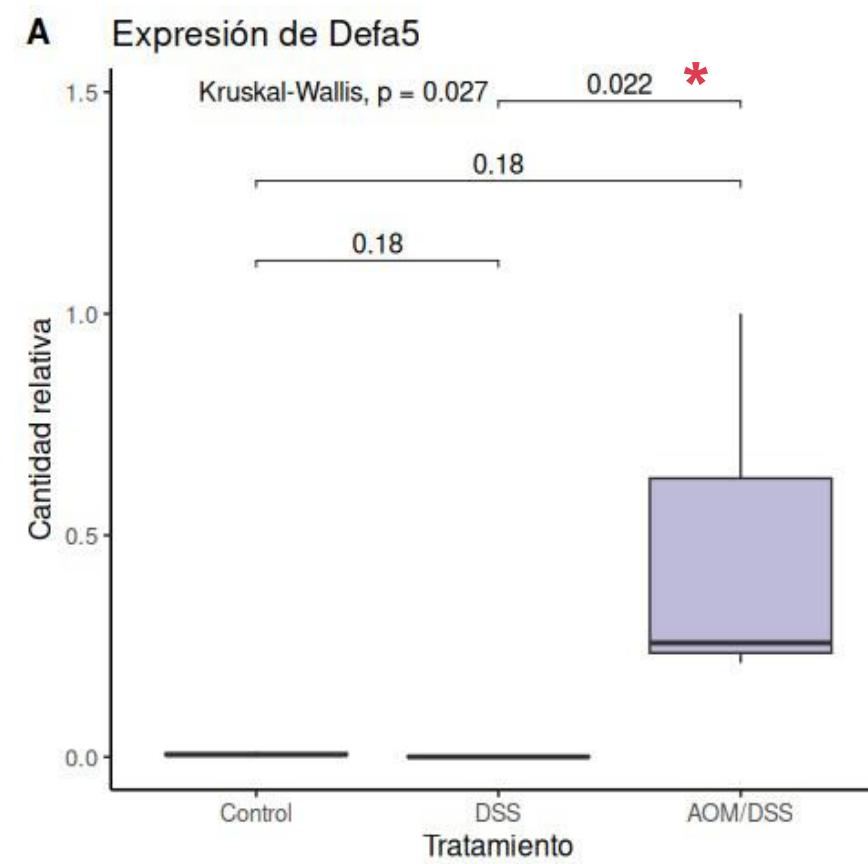
1. Control: No treatment
2. Acute Colitis: DSS
3. CCRAC: AOM-DSS



Dr. Mora Massaro
(DSS Intestinal
Inflammation Model)



Dr. Alejandro Cagnoni
(Model CCRAC by AOM-
DSS)

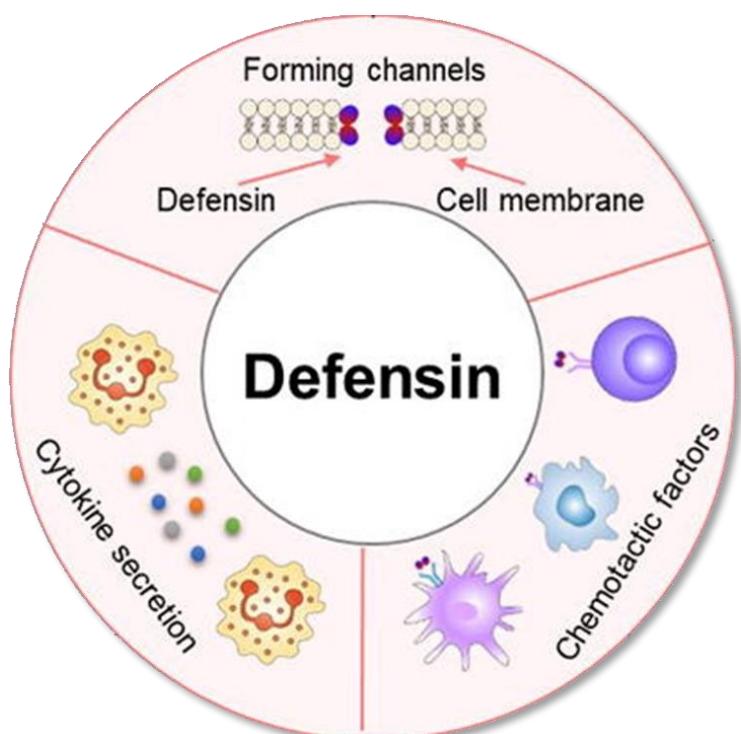
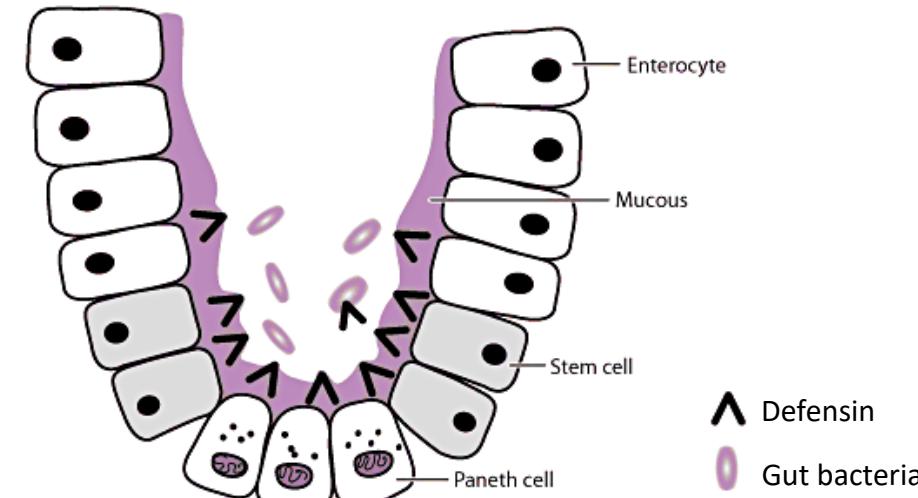


Results

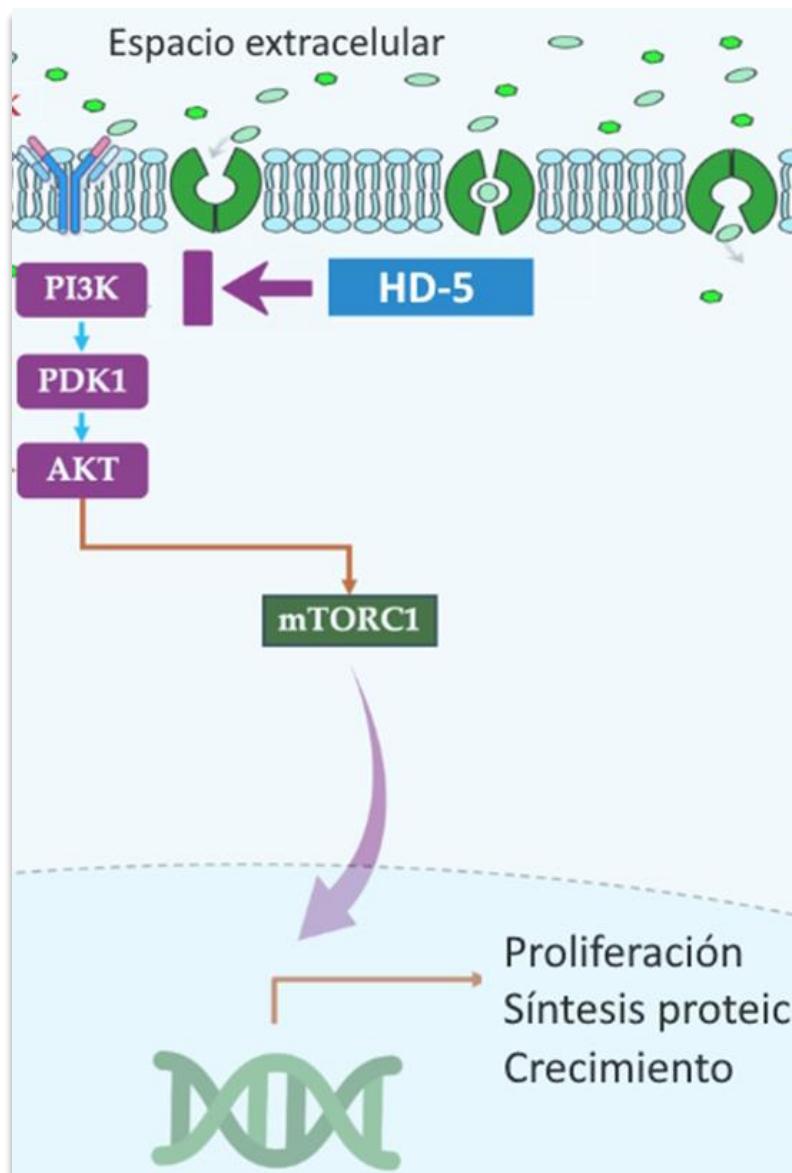


CONCLUSIONS AND DISCUSSION

DEFA5

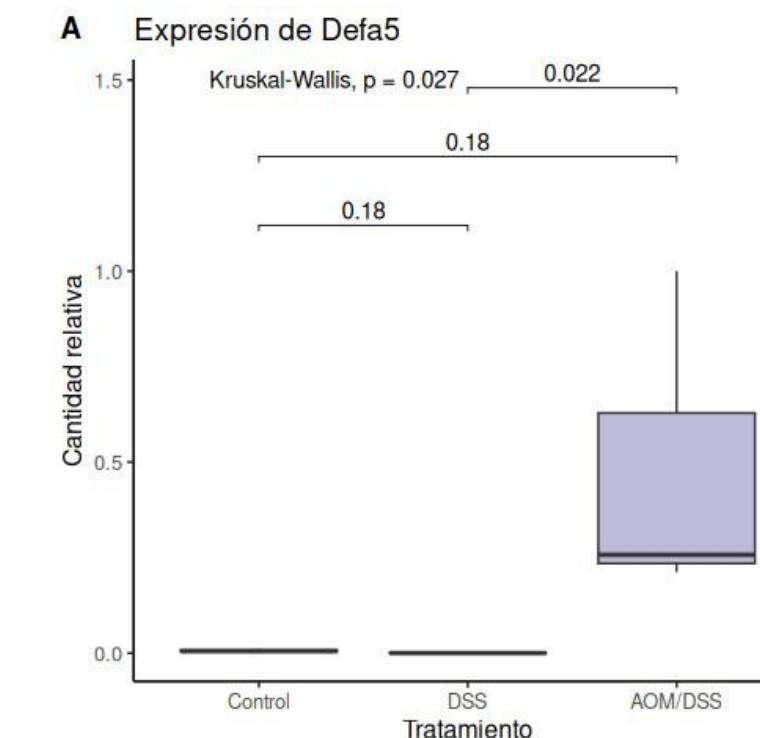


Gao et al (2021). Defensins: The natural peptide antibiotic. Doi: 10.1016/j.addr.2021.114008



Qiao et al (2021). Human α-defensin 5 suppressed colon cancer growth by targeting PI3K pathway. Doi: 10.1016/j.yexcr.2021.112809

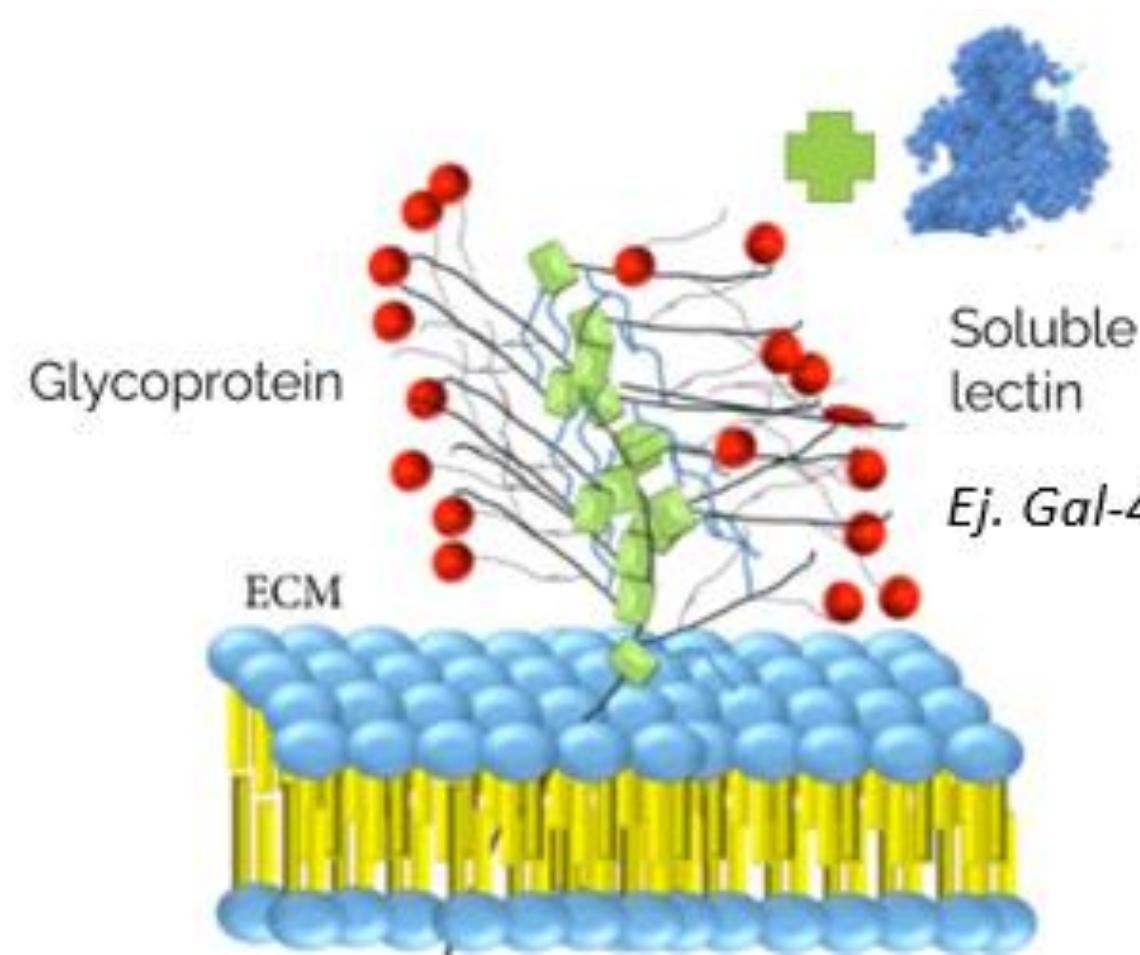
- Not expressed in healthy tissue
- ↑ in UC, proposed as a biomarker vs CD
- ↑ in CRC: associated with tumor suppression (blocking the PI3K pathway) and longer survival
- There are no studies in CCRAC



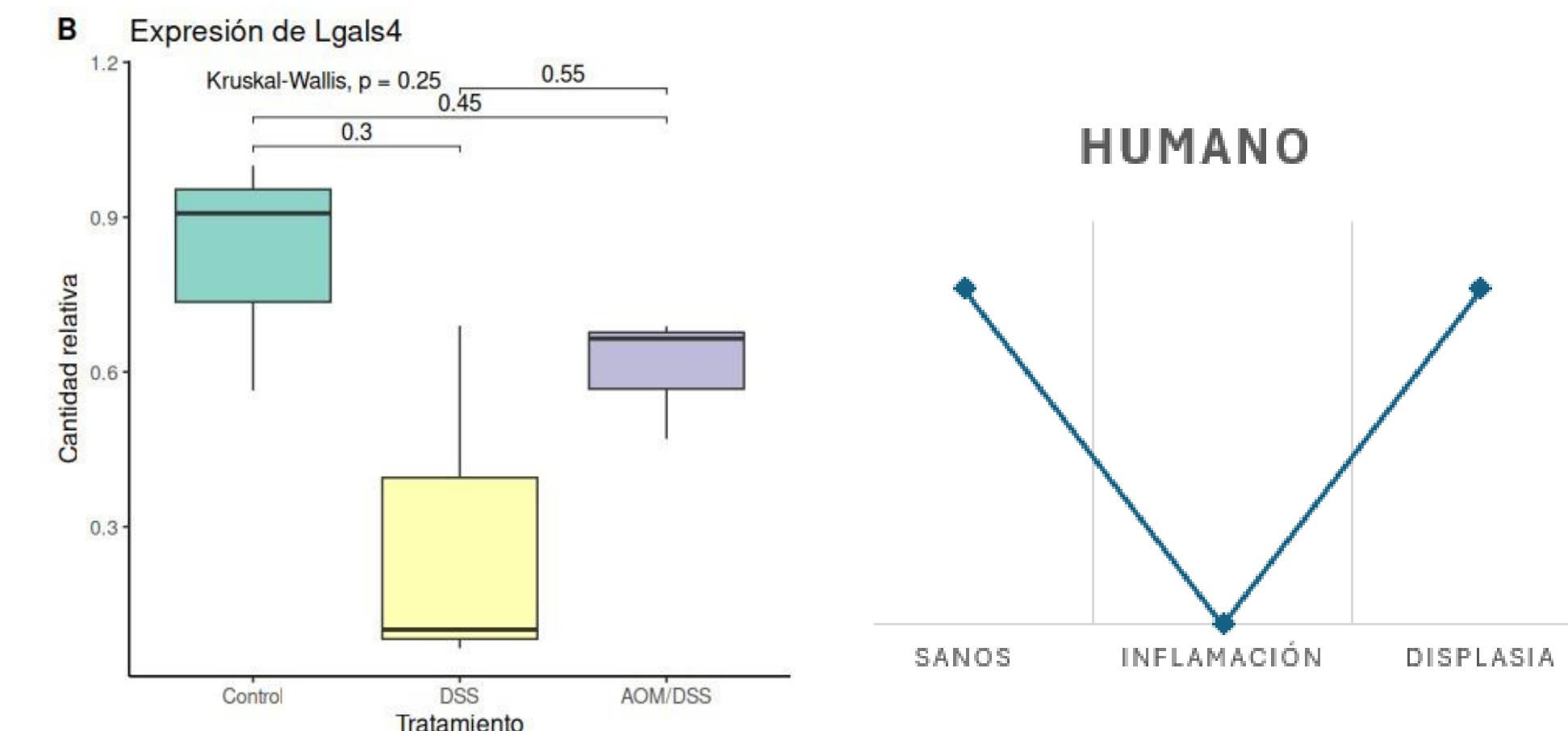
LGALS4



Galectins: Glycan-binding proteins with various roles; Therapeutic targets in neoplasia

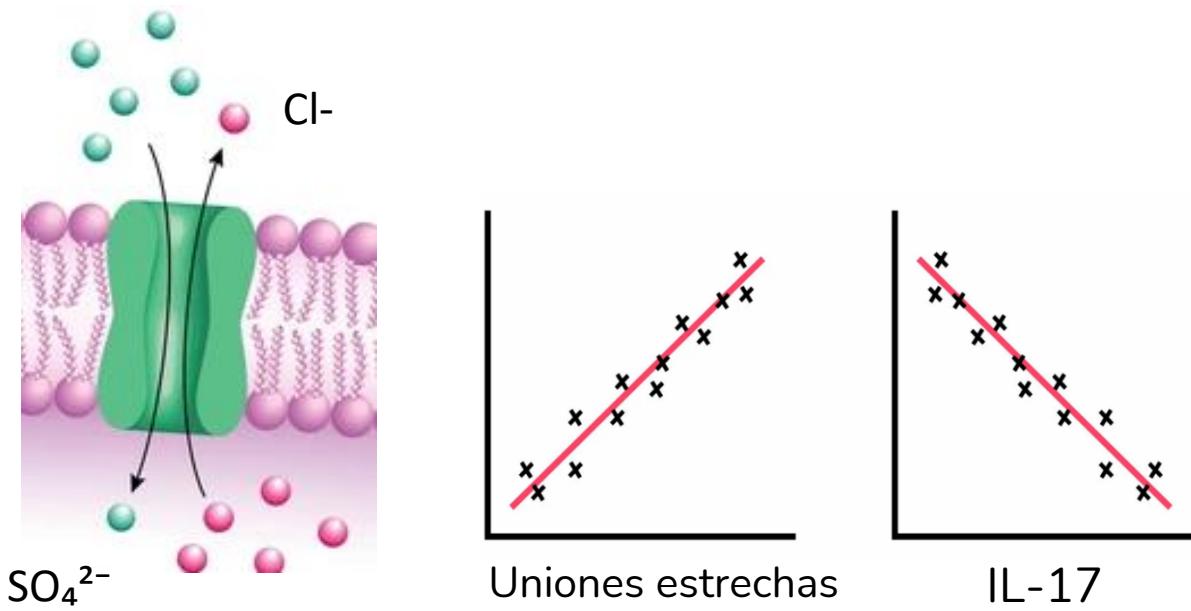


- Affects memory CD4+ T expansion
- ↓ in CRC tumors vs. healthy tissue

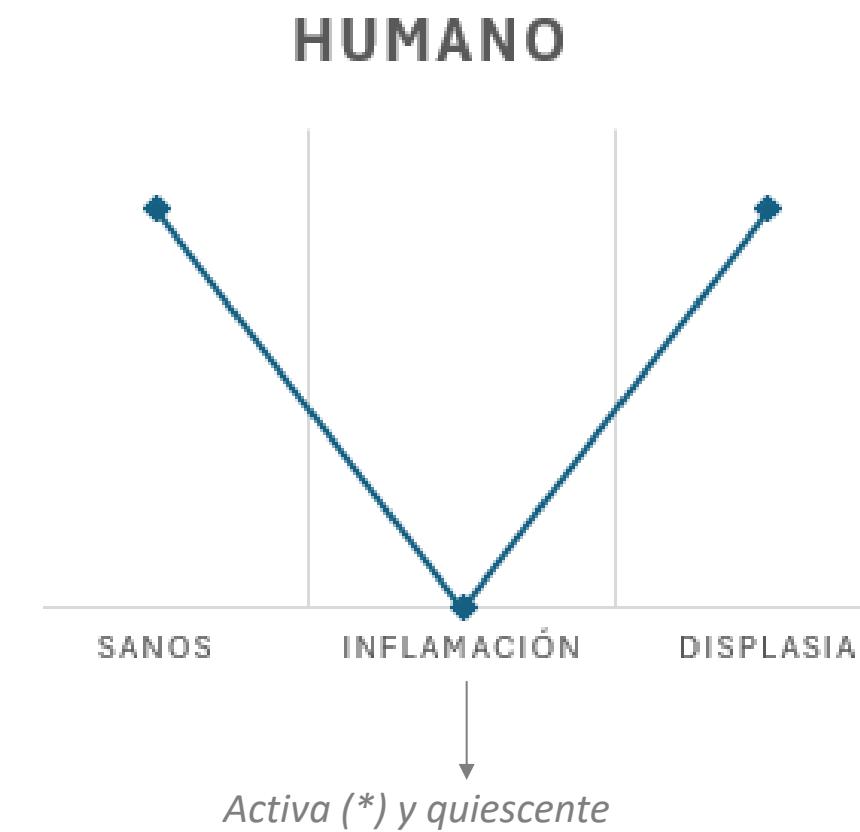
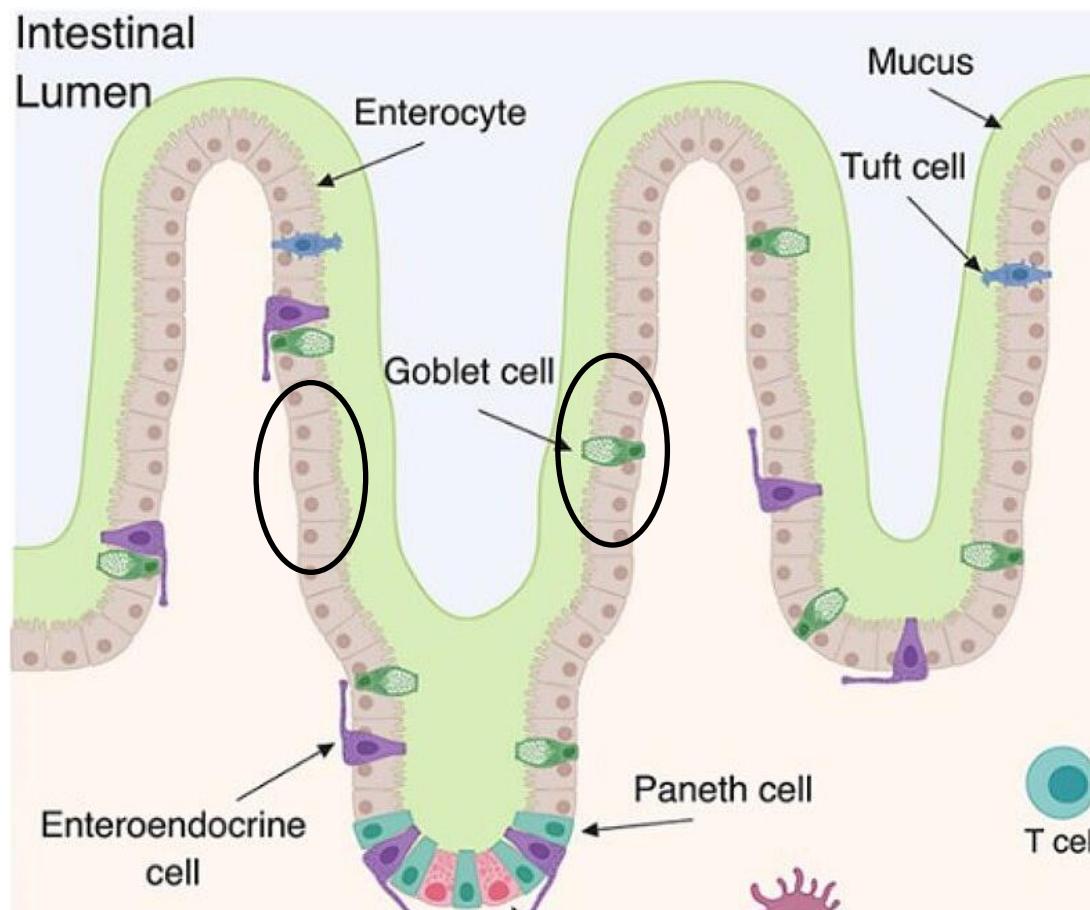


Conclusions and discussion

SLC26A2

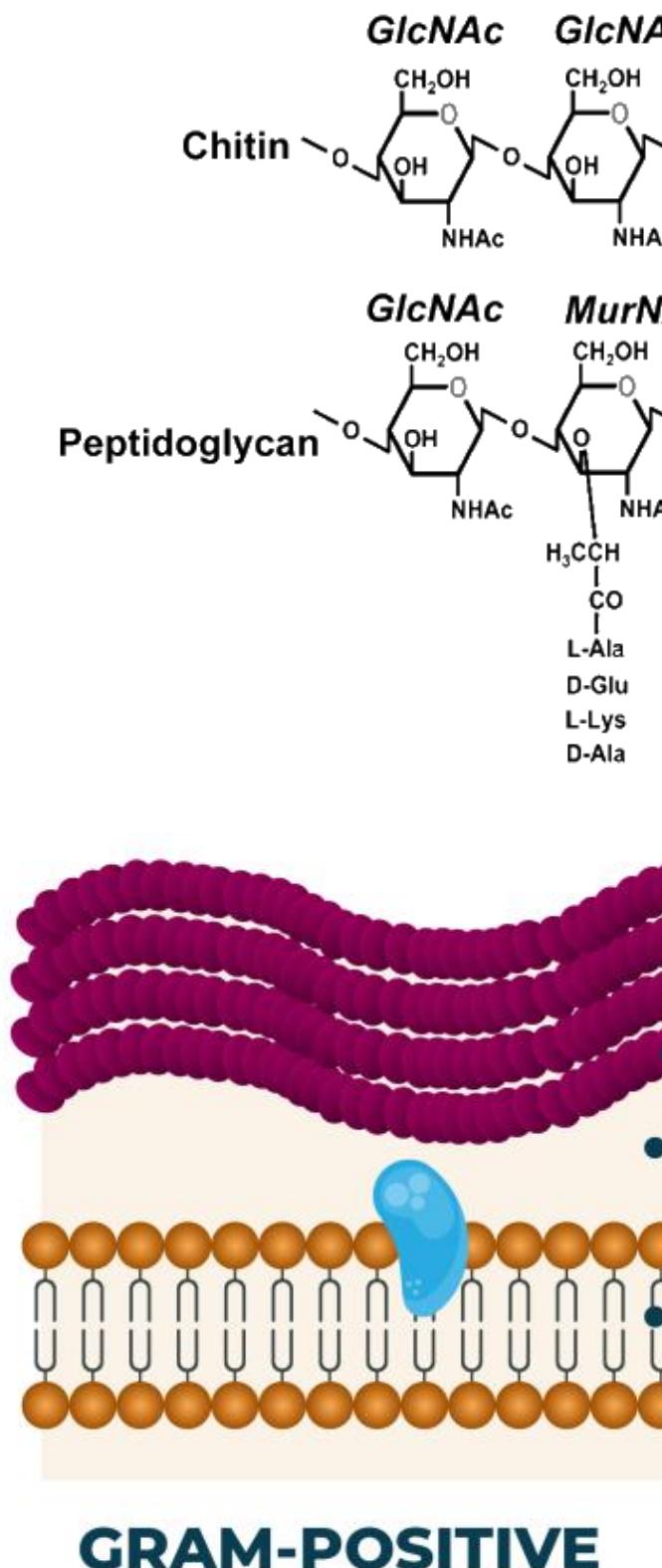


- ↓ on active UC and DSS models.
- Regulates mucins
- ↓ in cancer: worse prognosis, greater proliferation

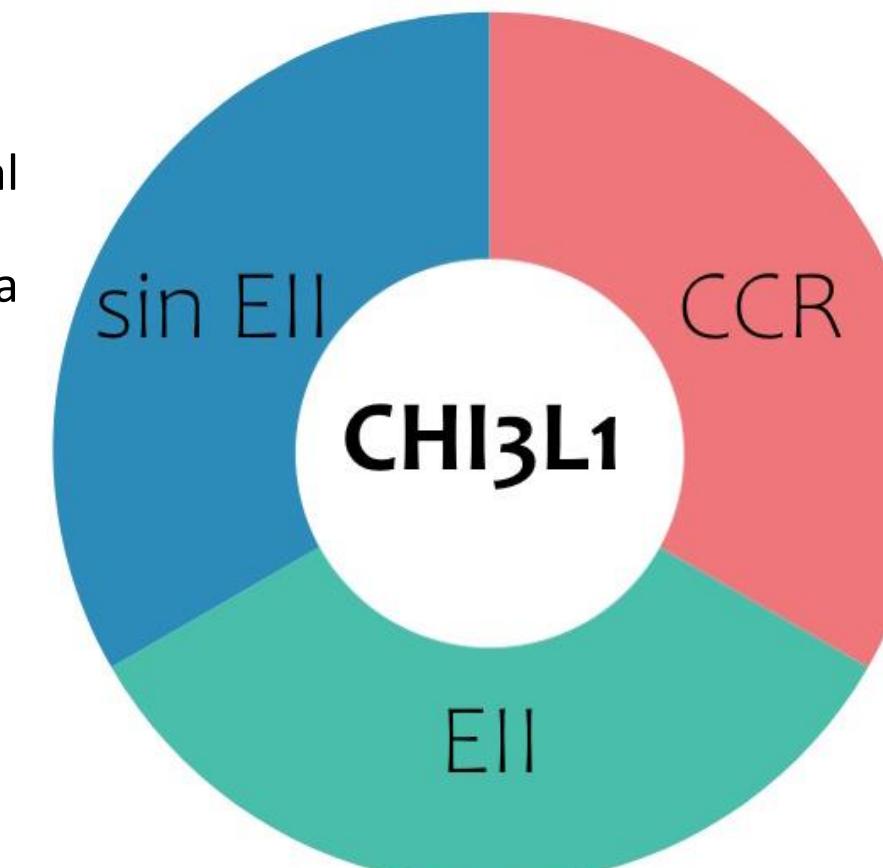


Conclusions and discussion

CHI3L1

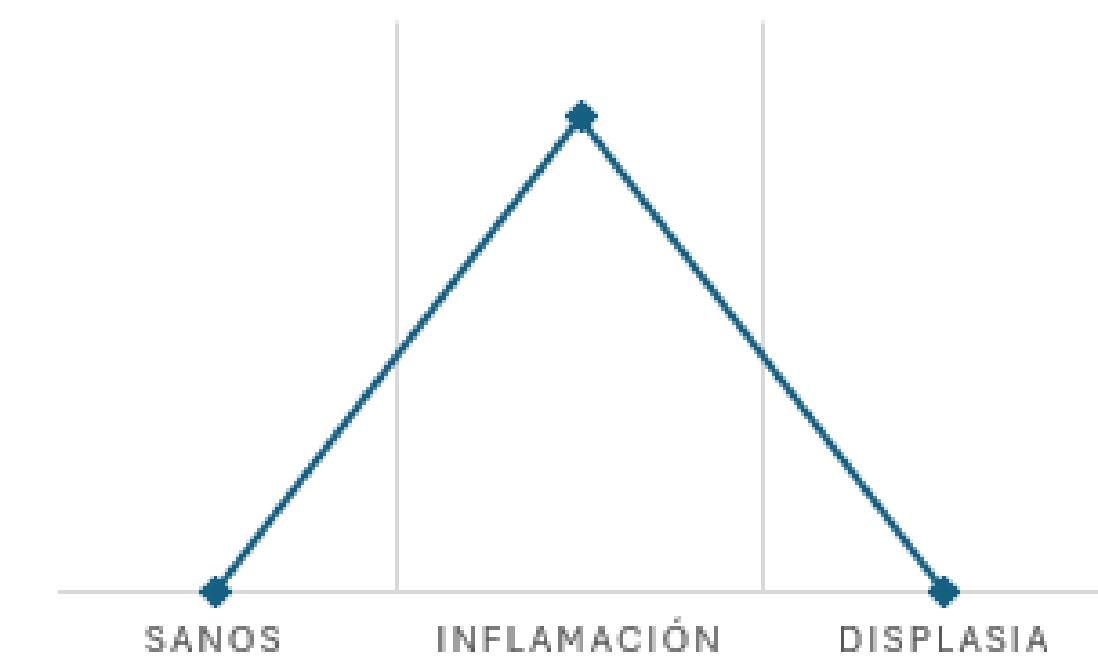


Anchoring commensal bacteria



- ↑ in serum (secreted by tumors)
- Promotes neoplastic development: Wnt/β-catenin

HUMANO



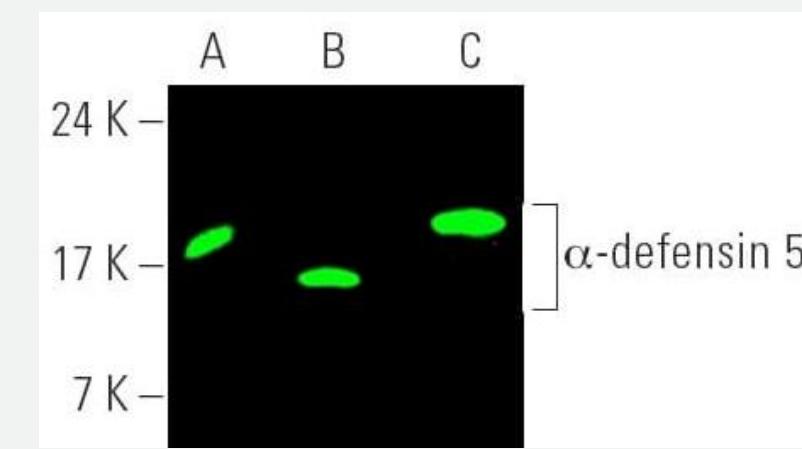
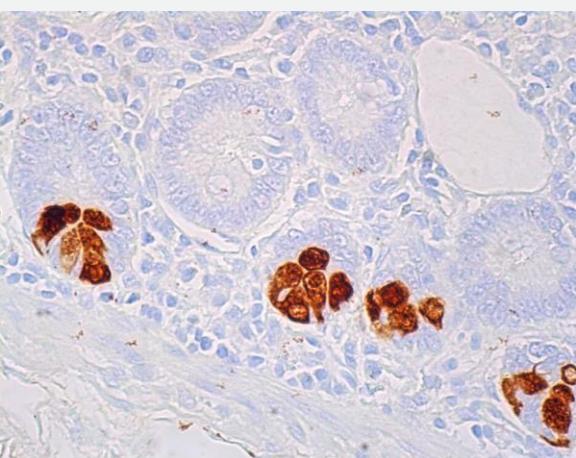
Conclusions and discussion

- ↑ in serum (CU)
- Expression associated with immune cells
- Chronic inflammation: Wnt/β-catenin
- ↓ Chi3l1 = ↑ DSS-induced colitis

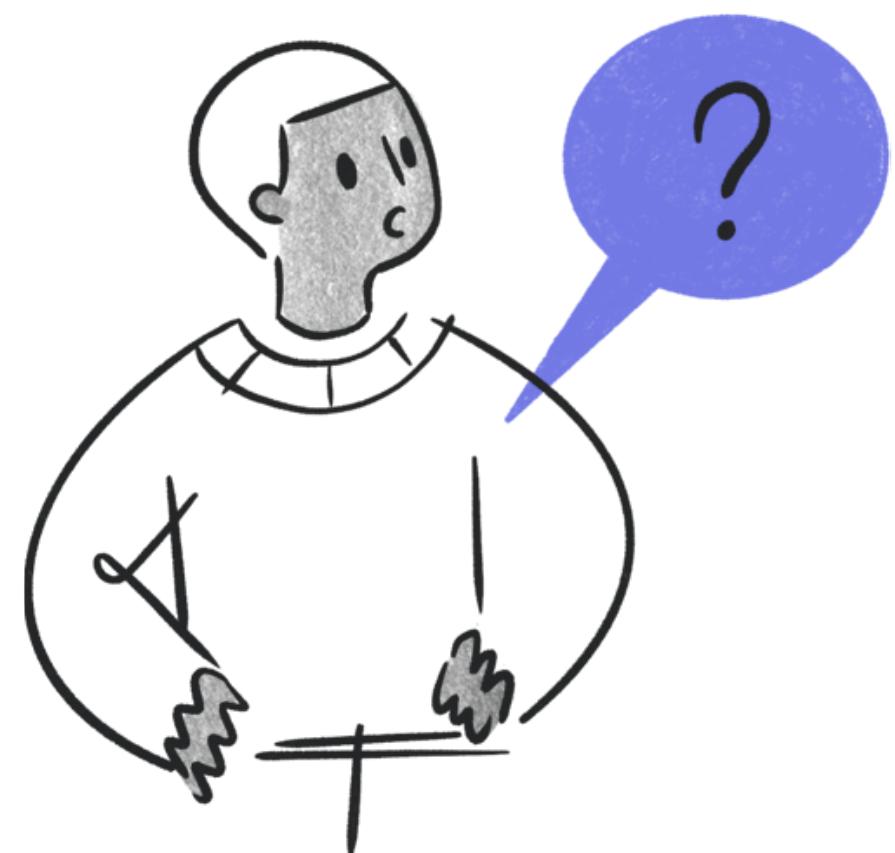
APORTES Y PERSPECTIVAS FUTURAS

- 1 A CCRAC/CU signature of 10 potentially dysregulated glycogenes was delineated, four of which (*Defa5*, *Lgals4*, *Lgals12*, and *St3gal1*) were analyzed by RT-qPCR, with significant results for ***Defa5***.
- 2 The glycobiological signature will be validated in a local cohort of patients, and through the use of single-cell technologies, the cellular origin of the dysregulation will be sought.
- 3 In the future, different methods of detecting DEFA5 expression that can be transferred to the clinic could be used. E.g. Western blot, and immunohistochemistry.

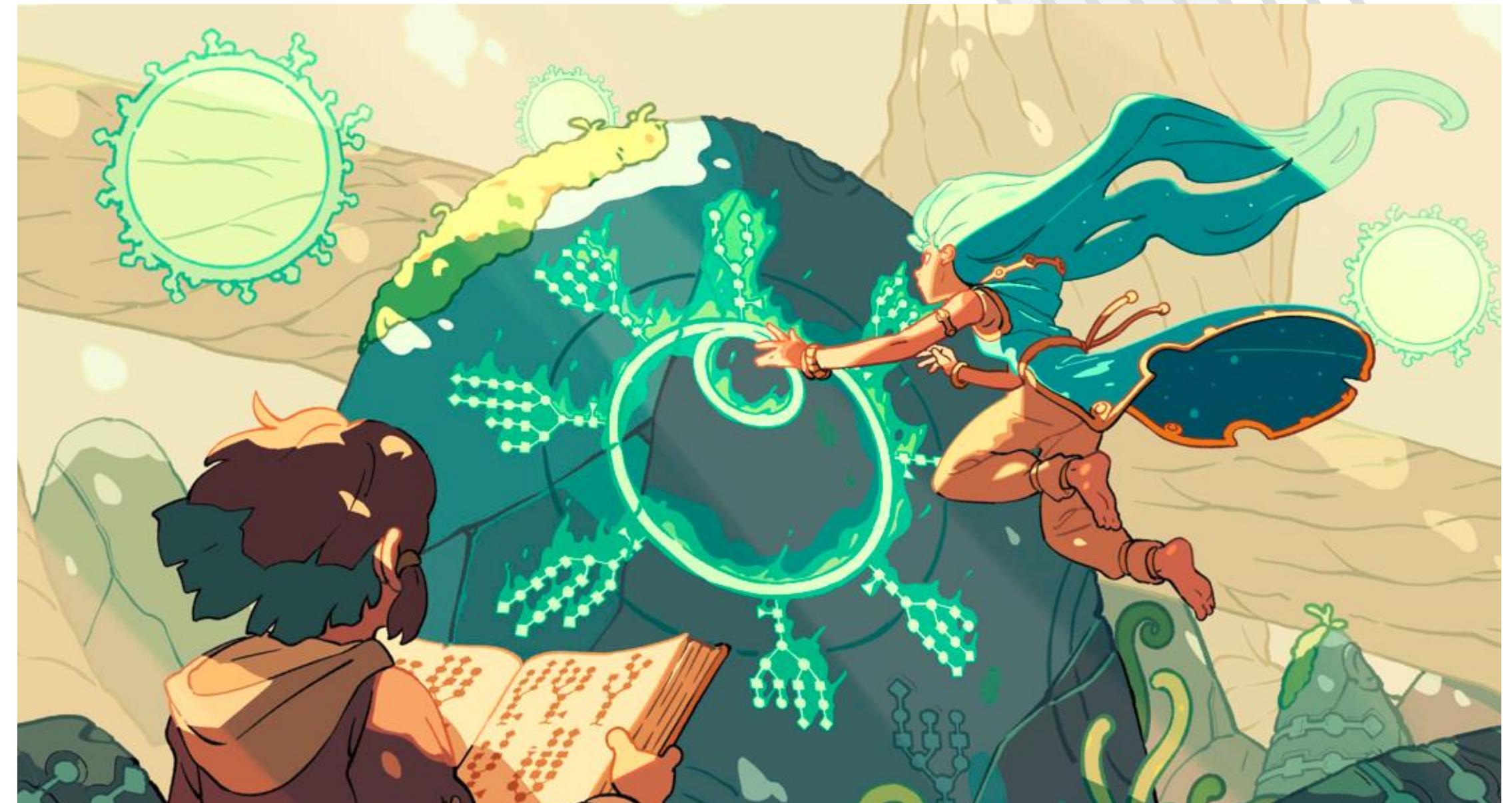
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THANK YOU VERY MUCH!



QUESTIONS?



UADE

CONICET


I B Y M E

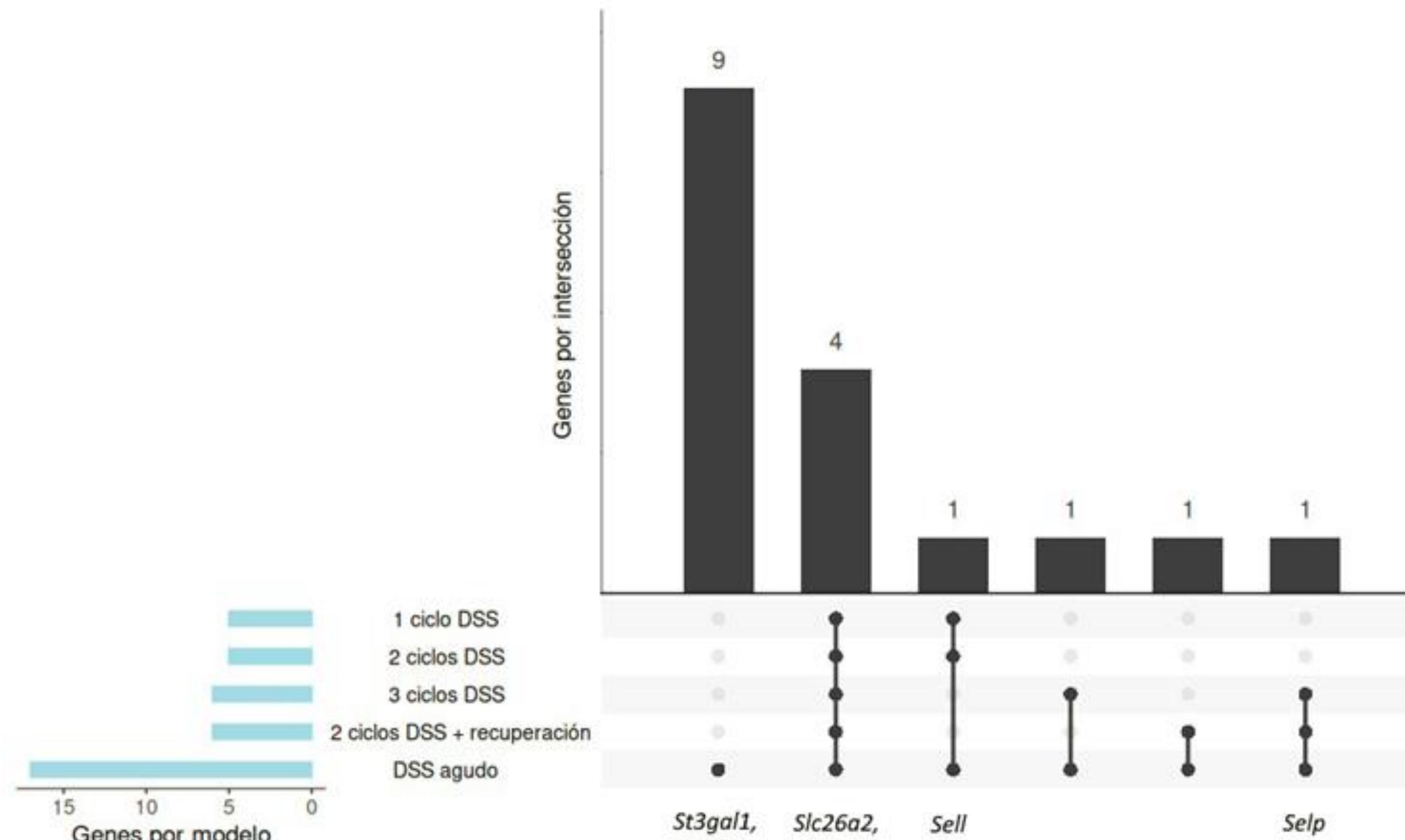


ADVANTAGES OF THE MURINE MODEL

Advantages	DSS / AOM-DSS Model	Similarity/usefulness in humans
Implementation	Easy, reliable, adaptable (dose/times)	Allows the study of acute, chronic or recurrent colitis
Initial mechanism	Epithelial damage → ingress of bacteria/antigens → inflammation	~ barrier dysfunction in IBD
Immune response	Acute phase: innate immunity (macrophages, neutrophils, TLR, TH1 cytokines: TNF- α , IFN- γ , IL-1 β , IL-12)	Reflects early immune mechanisms in IBD
Chronic colitis	Requires prolonged/cyclic DSS → TH2 cytokines (IL-4, IL-6, IL-10)	Reproduces changes in chronic human inflammation
Clinical manifestations	Diarrhea, weight loss, blood in the stool, anemia (acute phase)	Recapitulates various symptoms and clinical variability of IBD
Histopathology	Epithelial damage, ↓ mucins, neutrophilic infiltrate, crypt disorder...	Very similar to findings in human IBD
AOM-DSS Model	Tumors from 10 weeks, distal tumors, invasive adenocarcinomas	Reproduces key facets of human CACRC
Research Application	Useful for studying signalling (TLR4, IKK β , IL-6), influence of microbiota	Key to understanding the pathogenesis of CACRC



ACUTE OR CHRONIC?



× × × ×

Questions & Answers

LIMITATIONS OF THE MURINE MODEL

Limitations	CACRC	AOM/DSS
Injuries	Flat, invisible, require dyes	Raised polyps
Common mutations	TP53	APC (~ CCRE)
Carcinogenesis Time	Years	Weeks
Progression mechanism	Field cancerization: progressive accumulation, multifocal lesions	"Big Bang": Simultaneous Multiple Mutations, Rapid Clonal Expansion

CD4-dnTGF β RII/AOM)

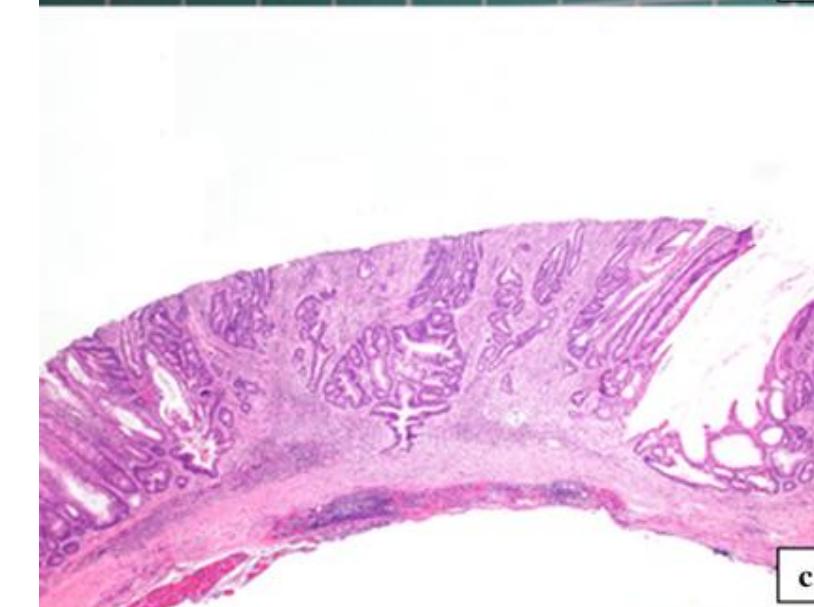


a

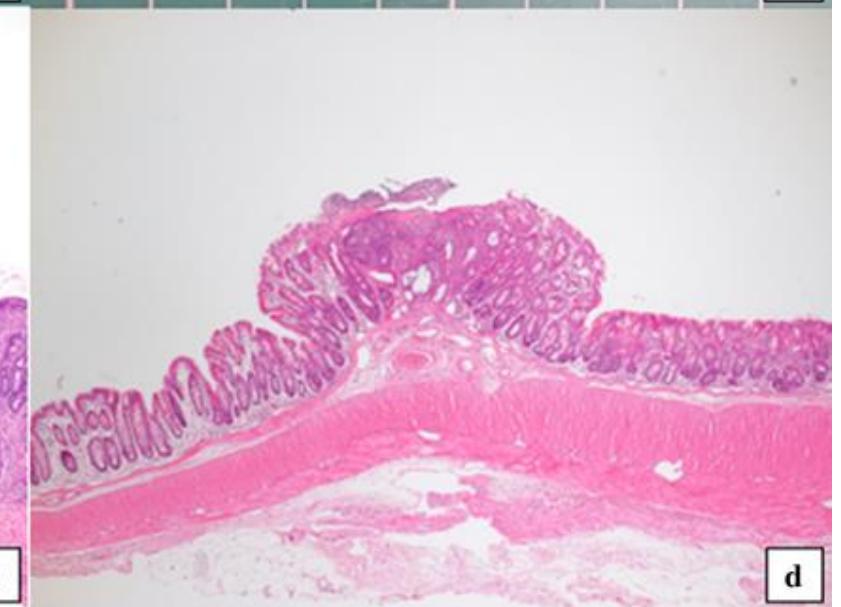
AOM/DSS



b



c



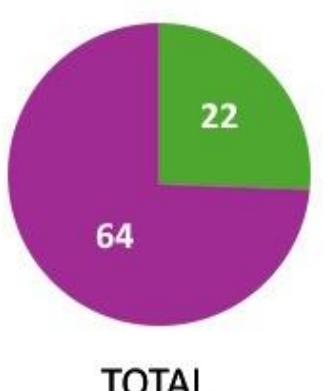
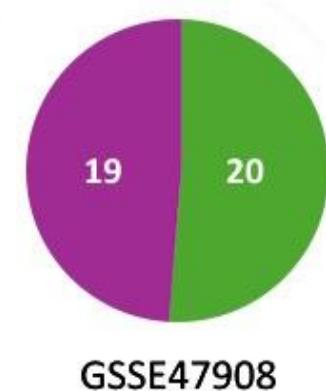
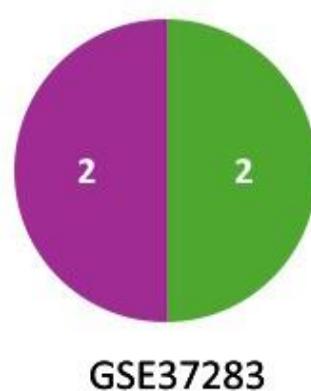
d

Hisamatsu, et al. Inflammation-Associated Carcinogenesis in Inflammatory Bowel Disease: Clinical Features and Molecular Mechanisms. *Cells* **2025**, *14*, 567.



PATIENT COMPOSITION

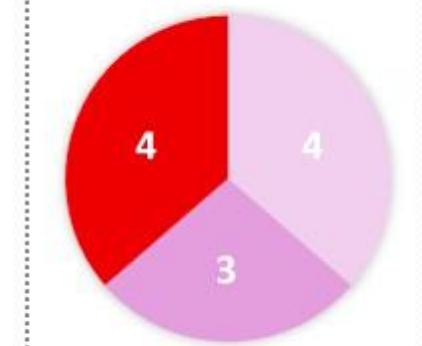
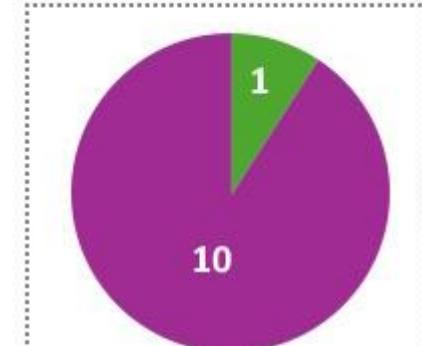
Pacientes con EII únicamente



Referencias

● Pancolitis (E3)	● LGD	● CU + LGD	● CU + CCRAC + LGD
● CU Izquierda (E2)	● HGD	● CU + HGD	● CU + CCRAC + HGD ● CU + CCRAC

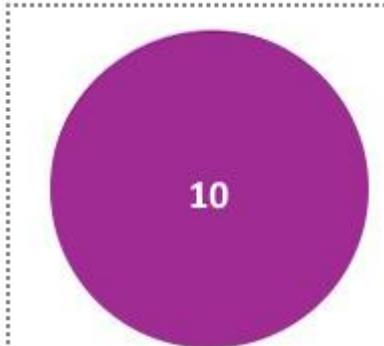
Pacientes con EII + displasia o cáncer



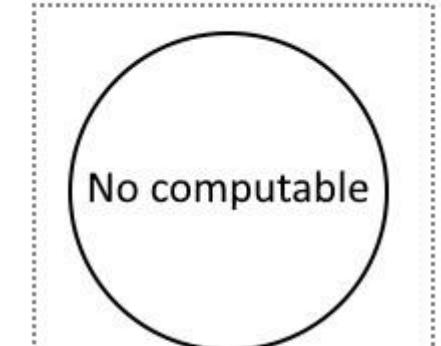
GSE37283



GSSE47908



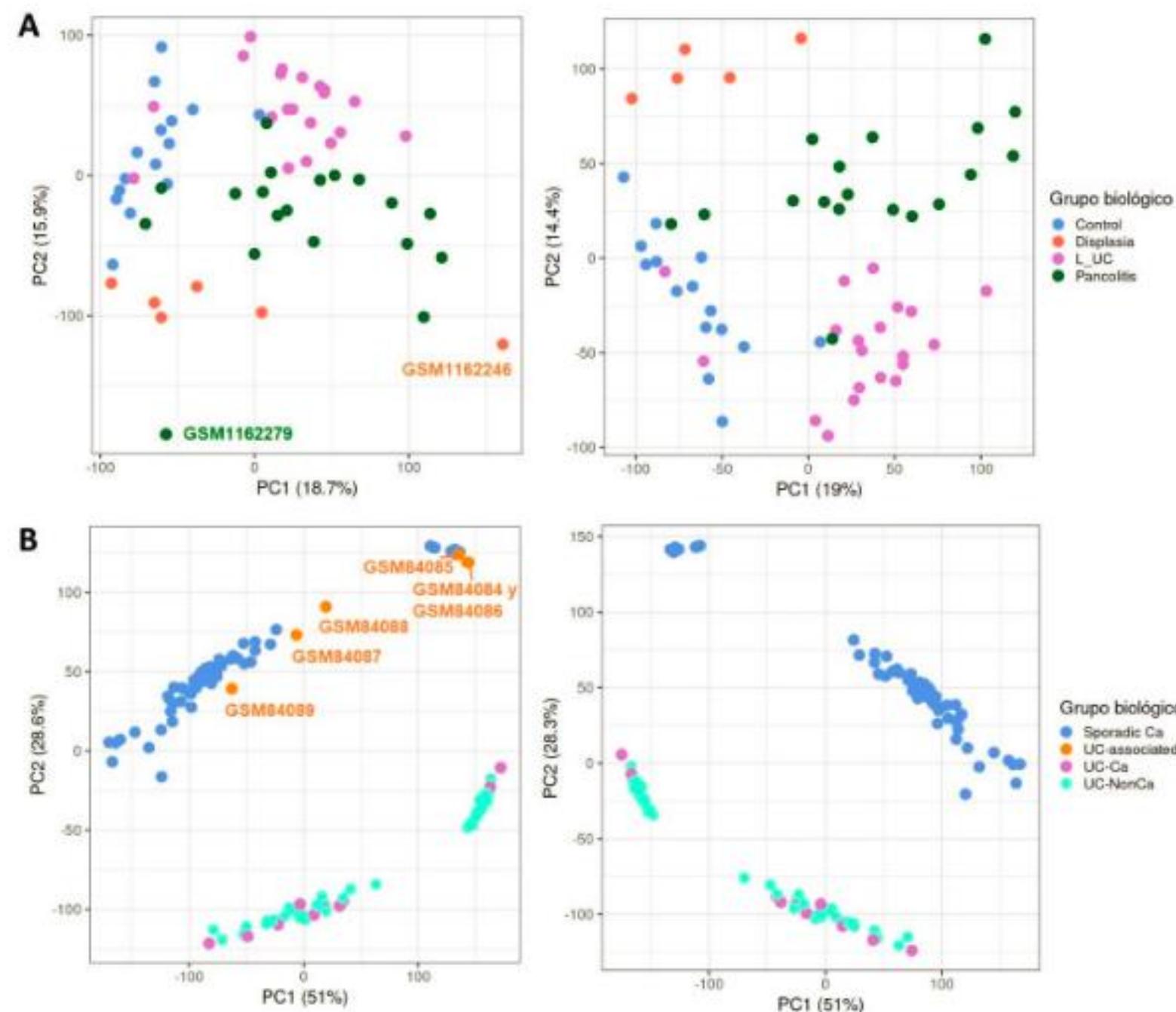
GSE3629



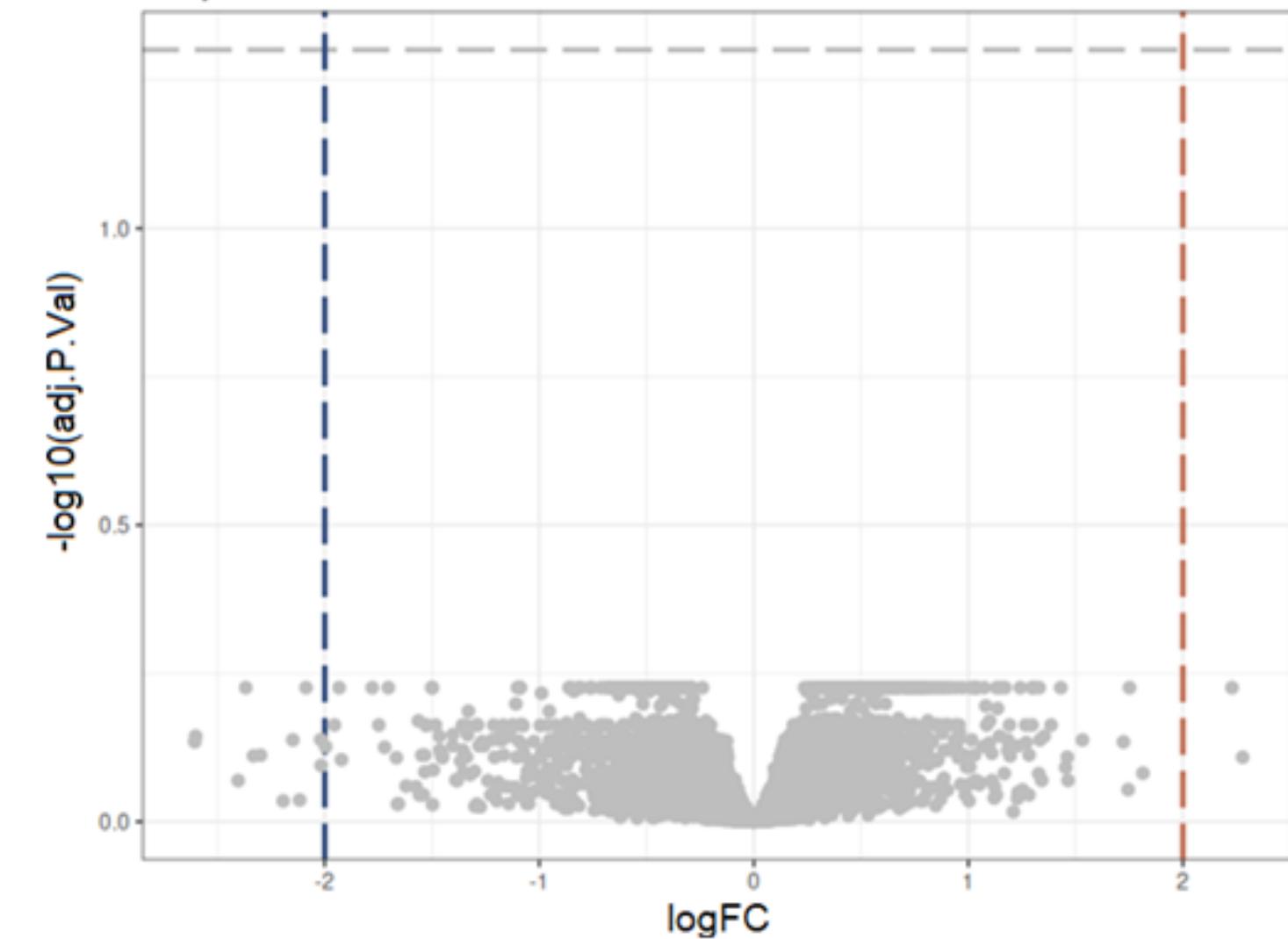
TOTAL



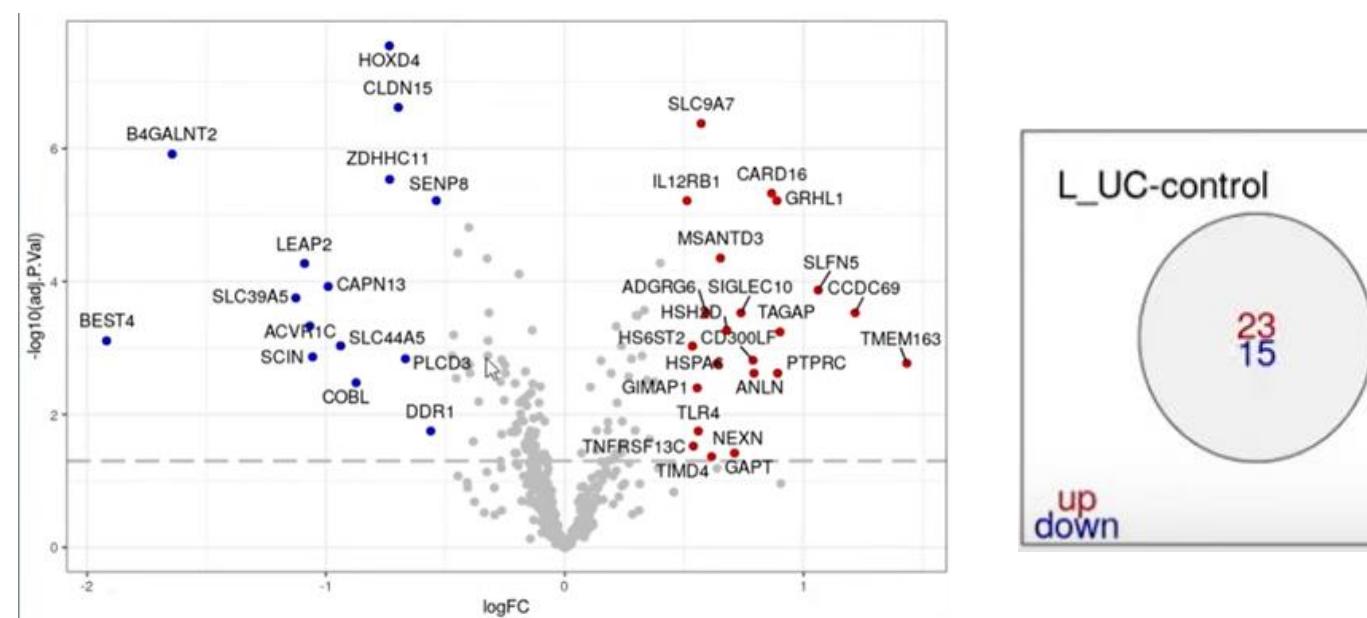
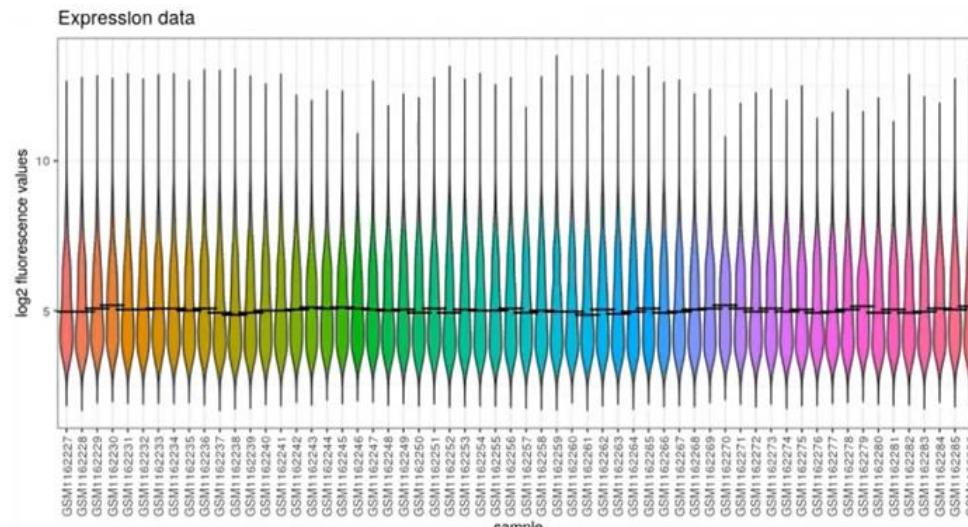
QUALITY CONTROL



Expresión diferencial de HGD vs. LGD



DEGFIND



```
> topTable(fit, coef=2, n=40, adjust="BH")
      ID logFC AveExpr      t P.Value adj.P.Val     B
4282 IG_821_1300838_1300922_fwd_st -3.32    12.4 -23.1 7.2e-09  5.3e-05 8.017
5365             serA_b2913_st  2.78    12.2  15.8 1.6e-07  6.0e-04 6.603
1389             gltD_b3213_st  3.03    10.9  13.3 6.4e-07  1.6e-03 5.779
4625             lrp_b0889_st  2.30     9.3  11.4 2.3e-06  4.0e-03 4.911
```

Degfind

R package with 8 functions for differential expression analysis in bulk (RNA-seq and microarrays).

DEG_table: Generates differential expression table.

SDRs: Extracts names from significant SDRs, and generates a Venn diagram with the positively and negatively regulated ones.

`gene_names`: Extracts gene names from SDR table

`make_lm`: Processes expression data to generate a linear model returns Bayesian results and statistics.

`make_toptable`: Processes Bayesian statistics from a linear model to generate a data frame, and classifies low- and high-expression genes.

`plot_data_quality`: Generates and saves a violin plot to describe the quality of the expression data.

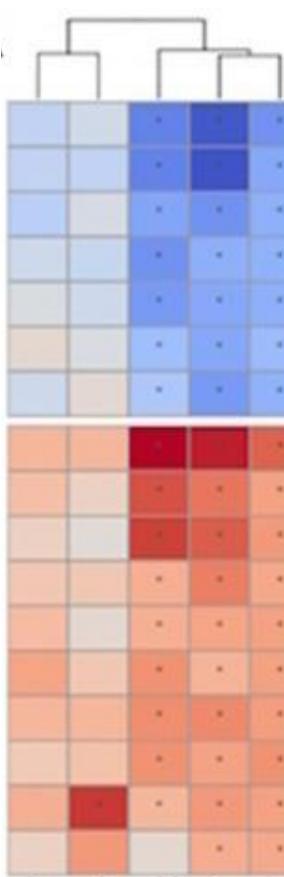
`sample_names`: Extracts names from the samples in the table.

volcano: Generates and saves a volcano plot with differential



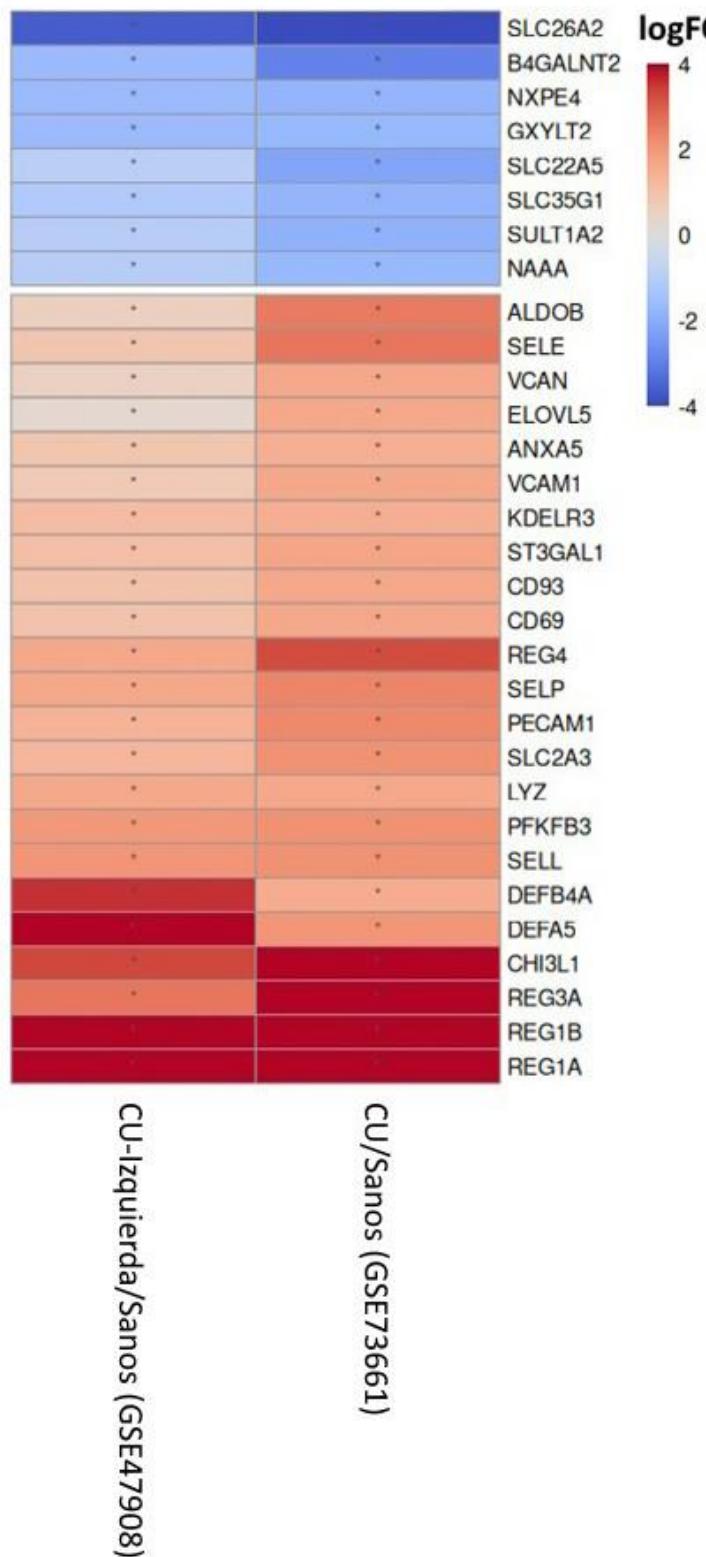
UC/HEALTHY

* *

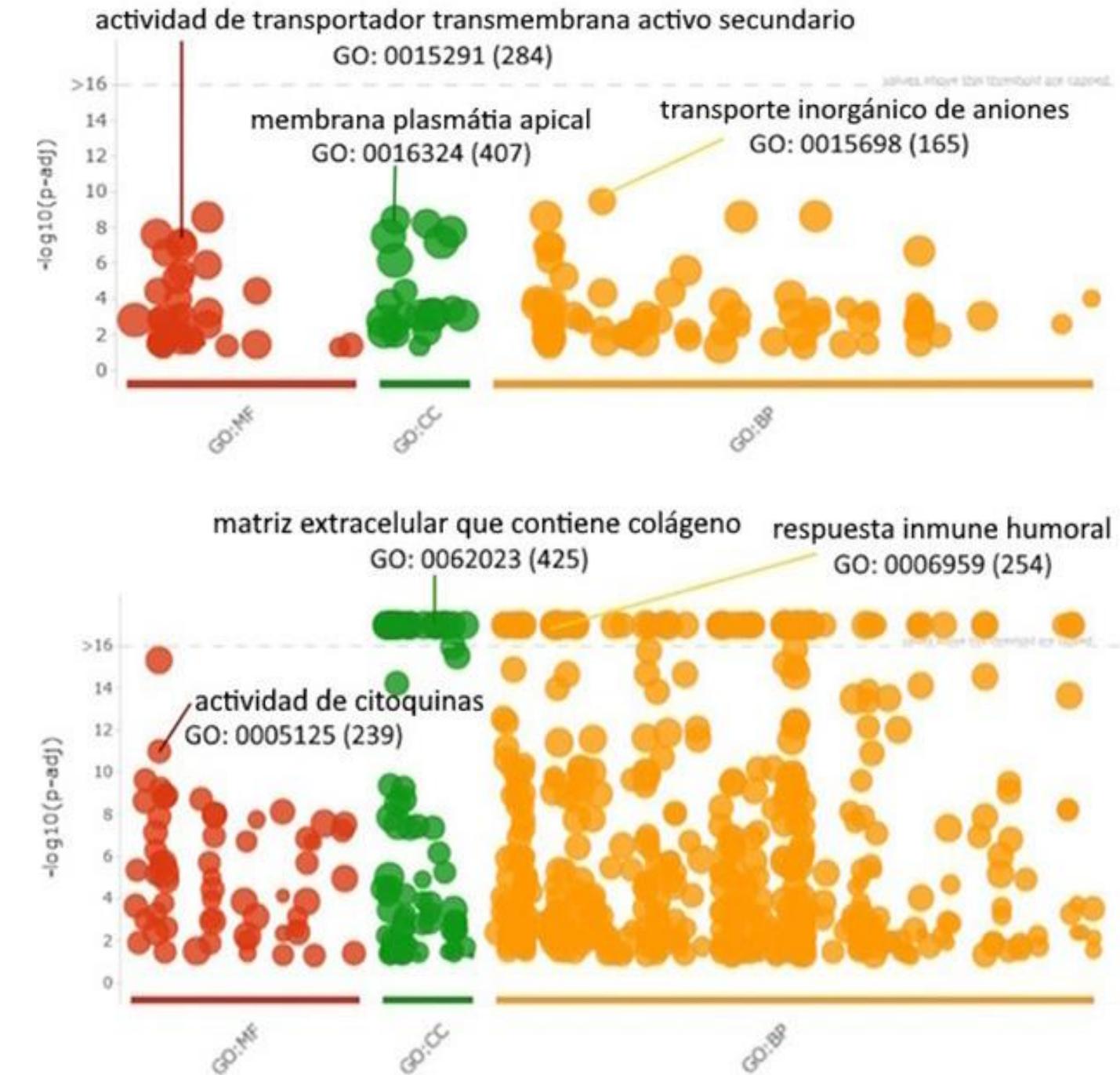


SLC26A2
HMGCS2
ADH1C
GUCA2B
CHP2
MS4A12
TRPM6
DUOX2
PI3
LCN2
TIMP1
MMP9
CXCL9
DMBT1
S100A9
OLF4
CCL2
CU/Sanos (GSE87473, GSE92415, GSE206285)
CU/Izquierda/Sanos (GSE73661)
CU/Sanos (GSE47908)
CU-Izquierda/Sanos (GSE27908)
CU-quiescente/Sanos (GSE37283)
CU/Sanos (GSE224758)

Glycogenes



Questions & Answers



IBYME MURINE MODEL

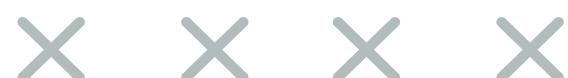


- C57Bl/6
- 8-12 weeks
- frozen in trizol
- 3 gut samples

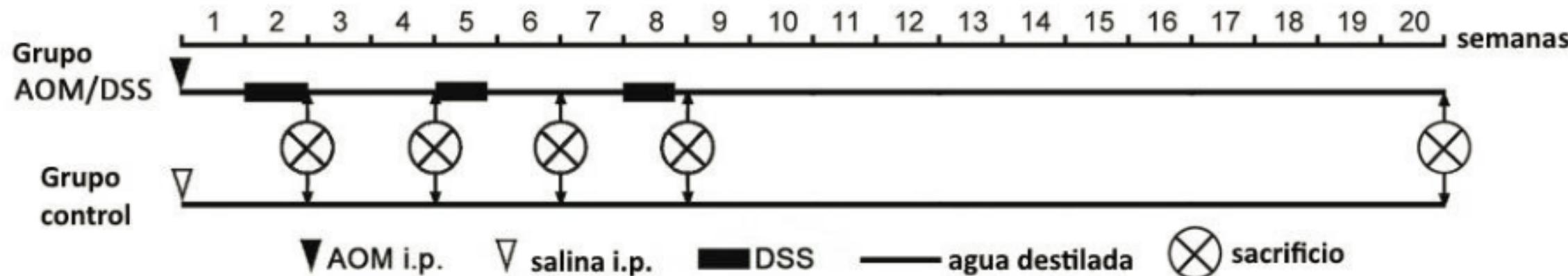
Control: untreated, frozen in September 2023. Galectin-4 flanked with a Loxp region, but its phenotype was wild (VillinCre^{wt}/wtLgals4 flox/phlox)

Acute Colitis (DSS): VillinCre^{wt}/wtLgals4flox/phlox treated with DSS 3% in drinking water for 5 days and then 5 days regular water. The total duration of the experiment was 10 days. The gut samples, inflamed or not, were frozen in February 2023.

CACRC (azoxymethane/DSS): intraperitoneal injection of azoxymethane (AOM, 12.5 mg/kg); then DSS (2.5%) 5 days later in drinking water for 5 days, followed by 14 days of rest with regular water (x3 = 12 weeks). The tumor samples were frozen in January 2024.



MURINE MODEL ANALYZED IN SILICO



Control: intraperitoneal injection of saline solution (10 mg/kg) on day 1, they drank distilled water. Sacrifice on the 14th.

Acute inflammation (AOM-DSS): week 2 (day 14). Intraperitoneal injection of AOM (10 mg/kg) on day 1, followed by three cycles of DSS administration (cycle 1: 2%, days 8~14) in drinking water.

CCRAC (AOM-DSS): Week 20 (day 140).. Intraperitoneal injection of AOM (10 mg/kg) on day 1, followed by three cycles of DSS administration (cycle 1: 2%, days 8~14; cycle 2: 1.5%, days 29~33; cycle 3: 1.5%, days 50~54) in drinking water.

× × × ×

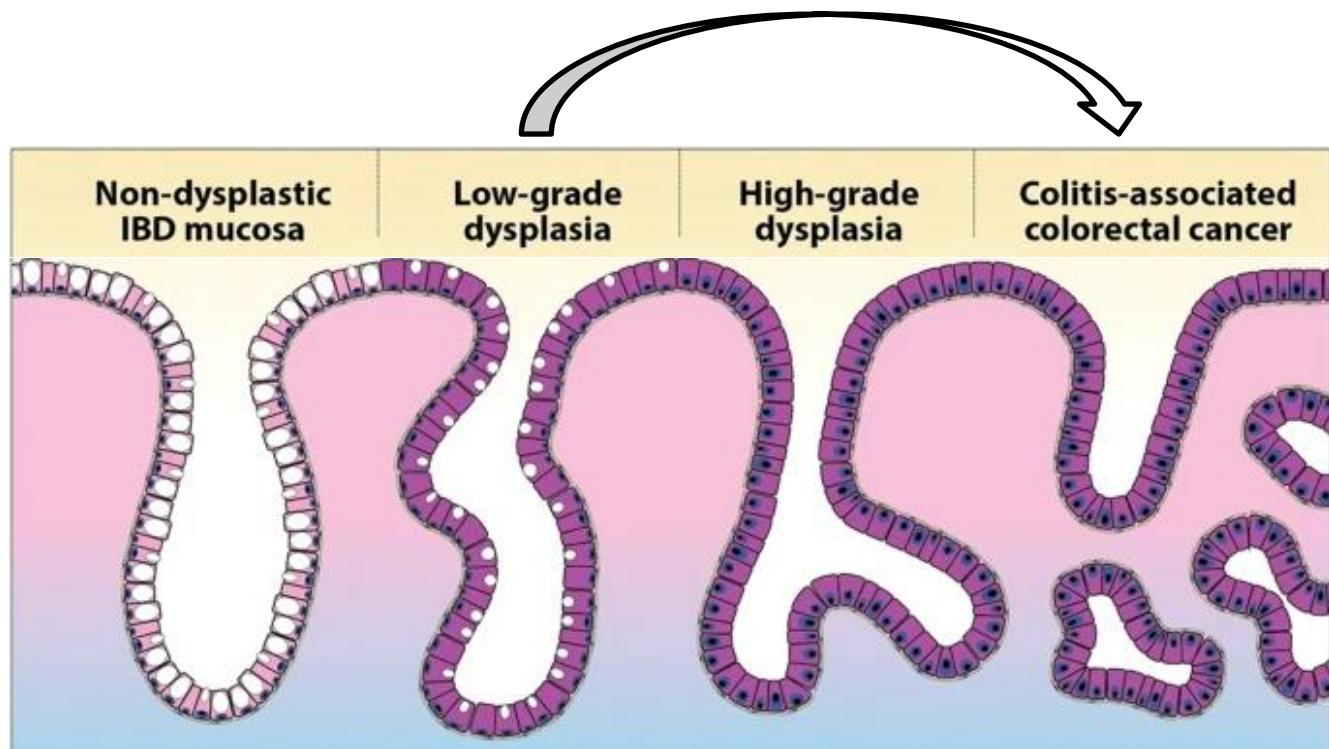
RT-QPCR

Gen	Nombre	Sentido	Secuencia
<i>B2m</i>	Beta-2-Microglobulina	FWD	ACCGTCTACTGGGATCGAGA
		REV	TGCTATTCTTCTGCGTGCAT
<i>Defa5</i>	Defensina Alfa 5	FWD	TTGTCCTCCTCTGCCCTGT
		REV	ATGAAGAGCAGACCCTTGTG G
<i>Lgals4</i>	Galectina-4	FWD	ATGGTCACCCATCTGCAAGT
		REV	AAGCTGGAATAGTCATGGCTCC
<i>Lgals12</i>	Galectina-12	FWD	AACTGACGAACACCTGGACC
		REV	TGCCATAAGGAATCACCGGG
<i>St3gal1</i>	ST3 beta-galactósido alfa-2,3-sialiltransferasa 1	FWD	TCCTACAAC TGCACACGCTCG
		REV	TGTTTCGCCTGGTGCCTGG

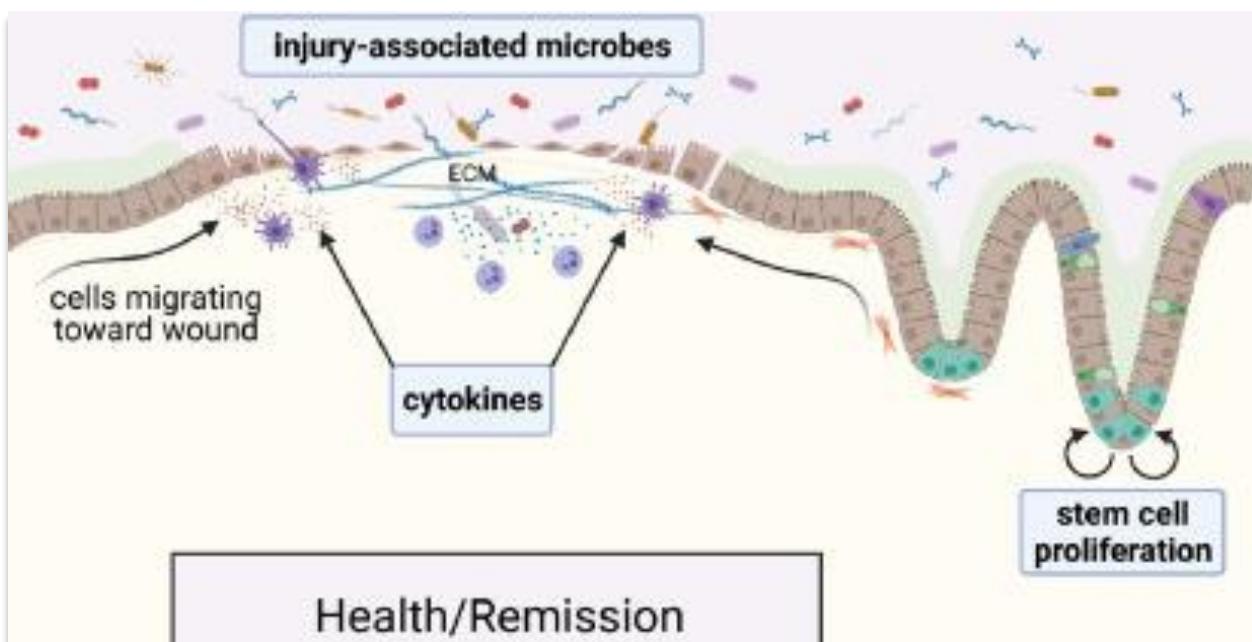
Gen	Efficiency (90-110)	Date
B2m	101.9	20/2
Defa5	121.1	20/2
Lgals12	-100	20/2
Lgals4	76.2	27/2
St3gal1	90.3	27/2

× × × ×

EXTENT OF INFLAMMATION AND DYSPLASIA

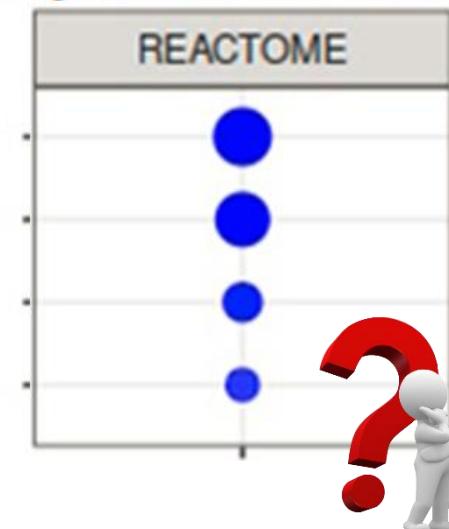


Zhou et al (2023). Molecular mechanisms in colitis-associated colorectal cancer. DOI:
10.1038/s41389-023-00492-0



Liu et al (2021). Epithelial wound healing in inflammatory bowel diseases: the next therapeutic frontier. DOI: 10.1016/j.trsl.2021.06.001

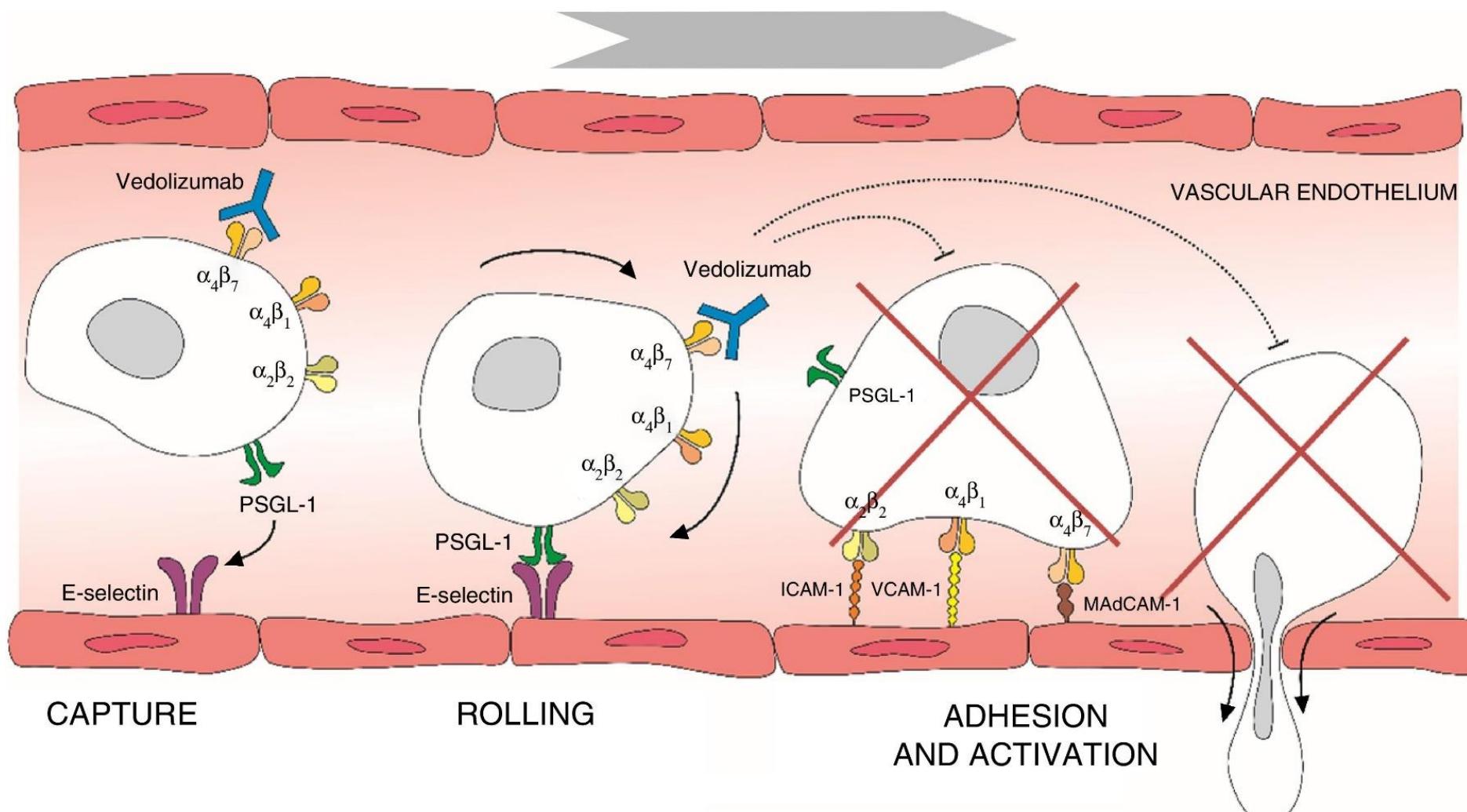
GSEA: dysplasia vs. CU-I



Single-cell

Bulk

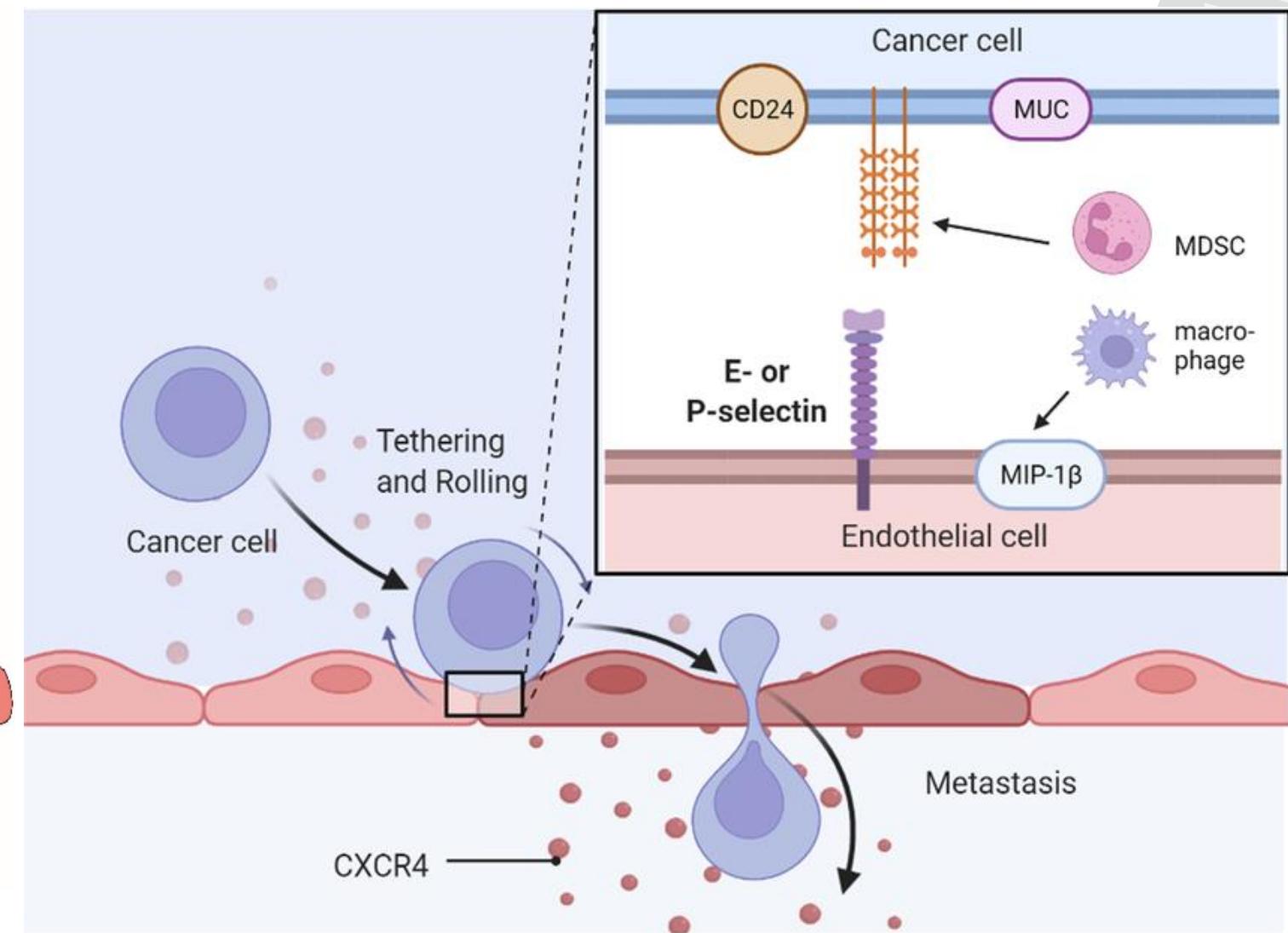
ADHESION MOLECULES: SELL, SELP, AND ICAM1



Domènech y Gisbert (2016). Efficacy and safety of vedolizumab in the treatment of ulcerative colitis. DOI: 10.1016/j.gastre.2016.11.008

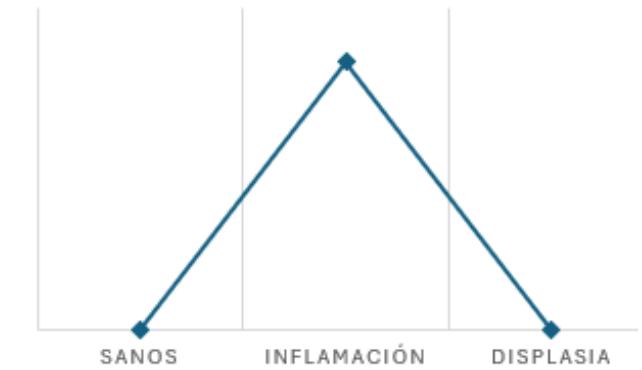
L-: leukocytes; P-: platelets and endothelial cells

ICAM1: immunoglobulin. Dual role in cancer: — secreted: worse prognosis; membrane: reduced tumor growth, increased survival (infiltration and cytotoxicity of antitumor CD8+ T cells)



Mechanisms of Cell Adhesion Molecules in Endocrine-Related Cancers: A Concise Outlook. DOI: 10.3389/fendo.2022.865436.

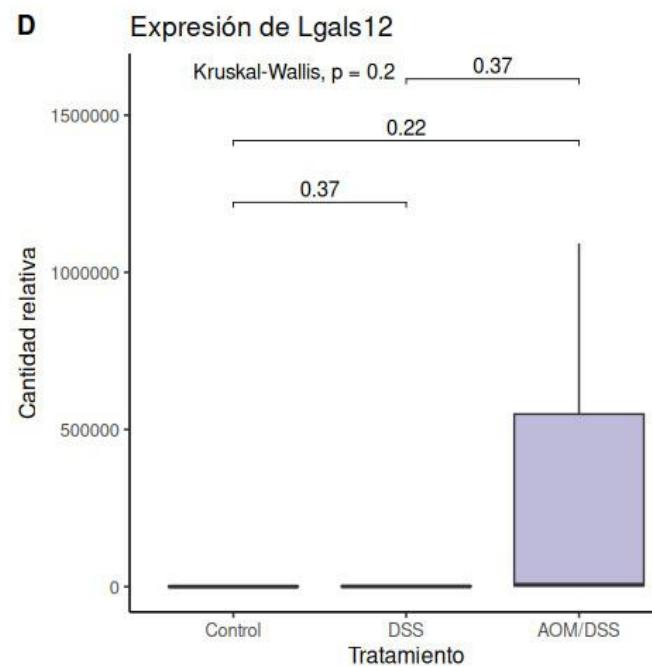
HUMANO





LGALS12, CHIA/CHIL3

Galectins: Glycan-binding proteins with various roles; Therapeutic targets in neoplasia



Lgals12:

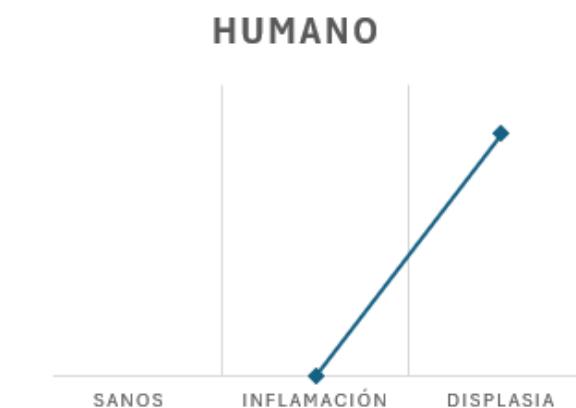
Possible role in inflammation (desensitized TNBS-induced colitis Gal12KO models)

Possible role in cell cycle control

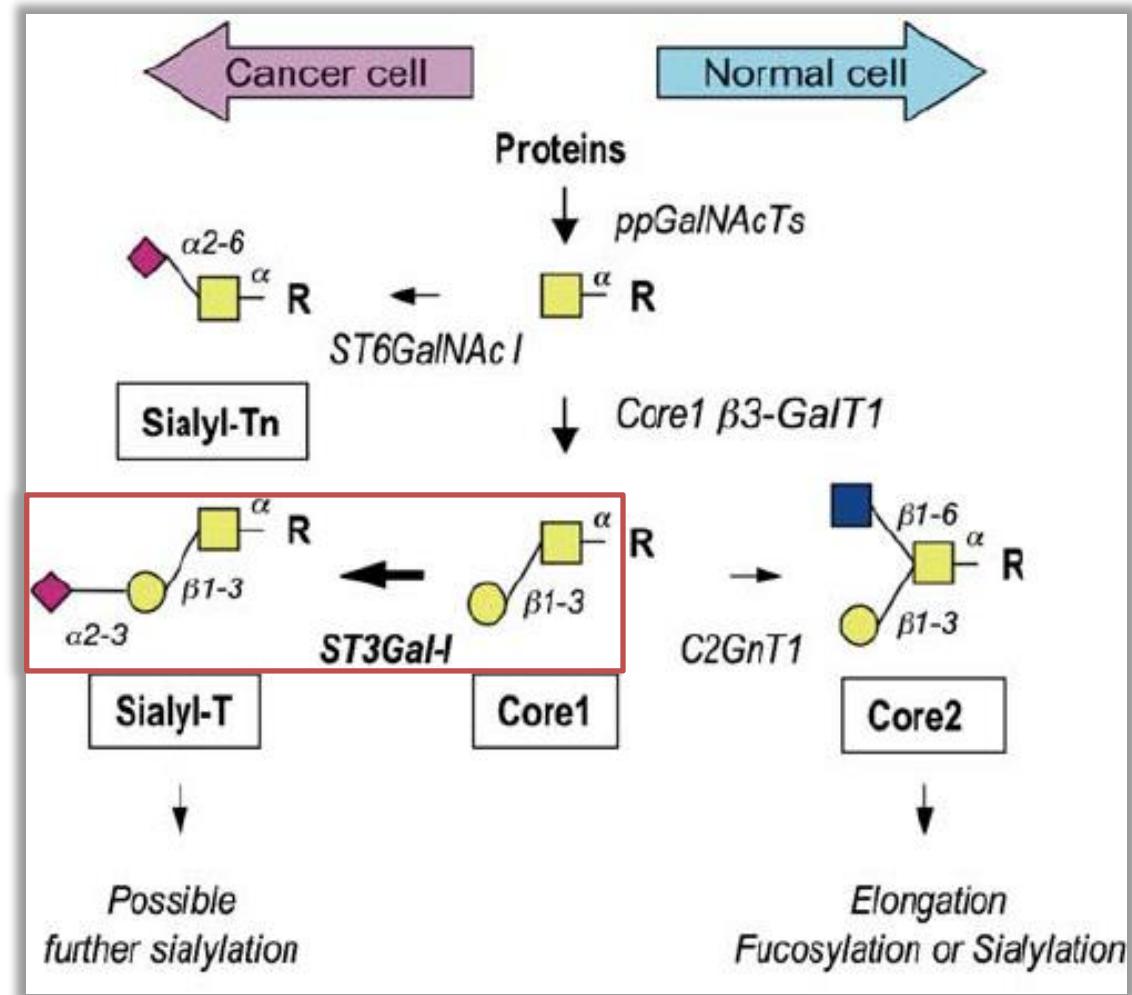
Silenced in CRC cell lines, with tumor suppression

CHIA/Chil3: mammalian acid chitinase (AMCase).

Pro-inflammatory: OAT-177 (selective inhibitor) in a model with DSS lowers inflammation

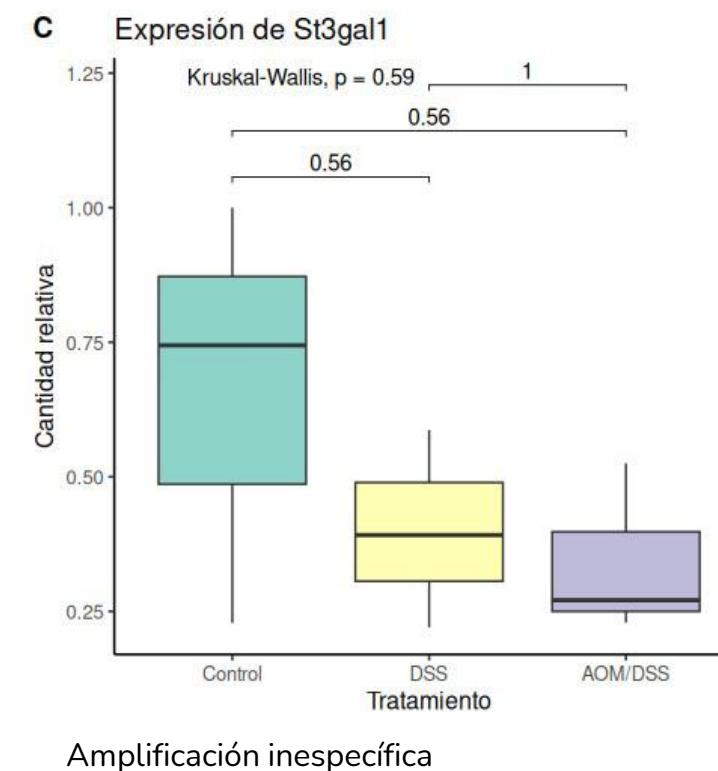


ST3GAL1

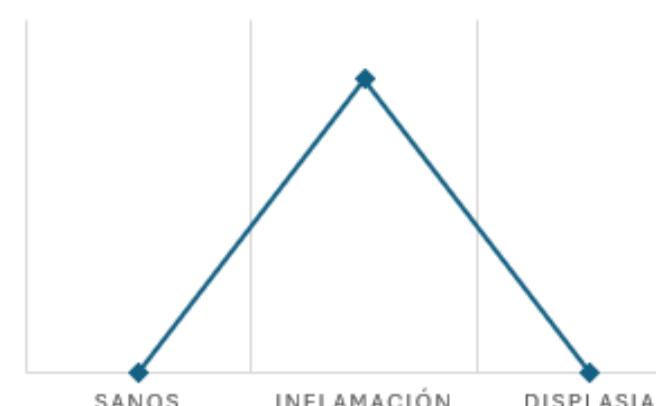


- [Yellow square] GalNAc N-acetylgalactosamine
- [Yellow circle] Gal Galactose
- [Pink diamond] Neu5Ac N-acetylneurameric acid (sialic acid)
- [Blue square] GlcNAc N-acetylglucosamine

Gianfranco et al (2010). Over-expression of ST3Gal-I promotes mammary tumorigenesis *Open Access*. *Doi: 10.1093/glycob/cwq085*



HUMANO



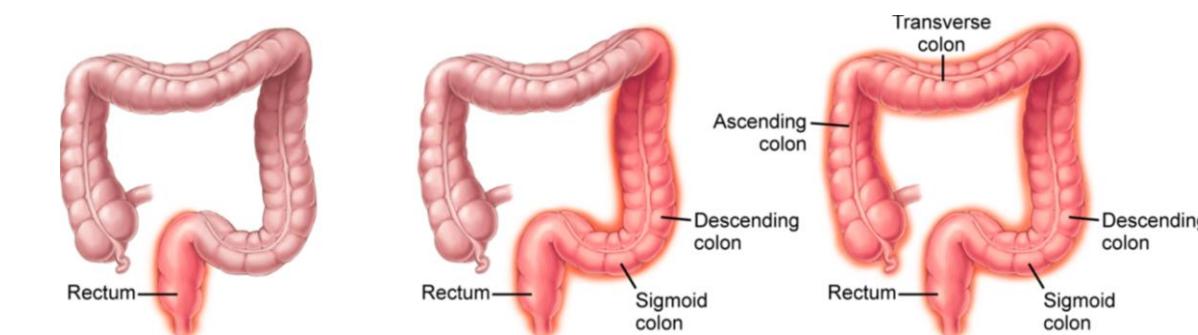
- Sialyl transferase: adds sialic acid, by means of a $\alpha(2,3)$ bond to galactose bound to N-acetylgalactosamine, which in turn is bound to serine or threonine in a protein (core O-type 1). This blocks the elongation of the chain.
- ↑ in cancer (CRC), where it promotes tumor invasion and metastasis, via the EGFR/NRP1 pathway



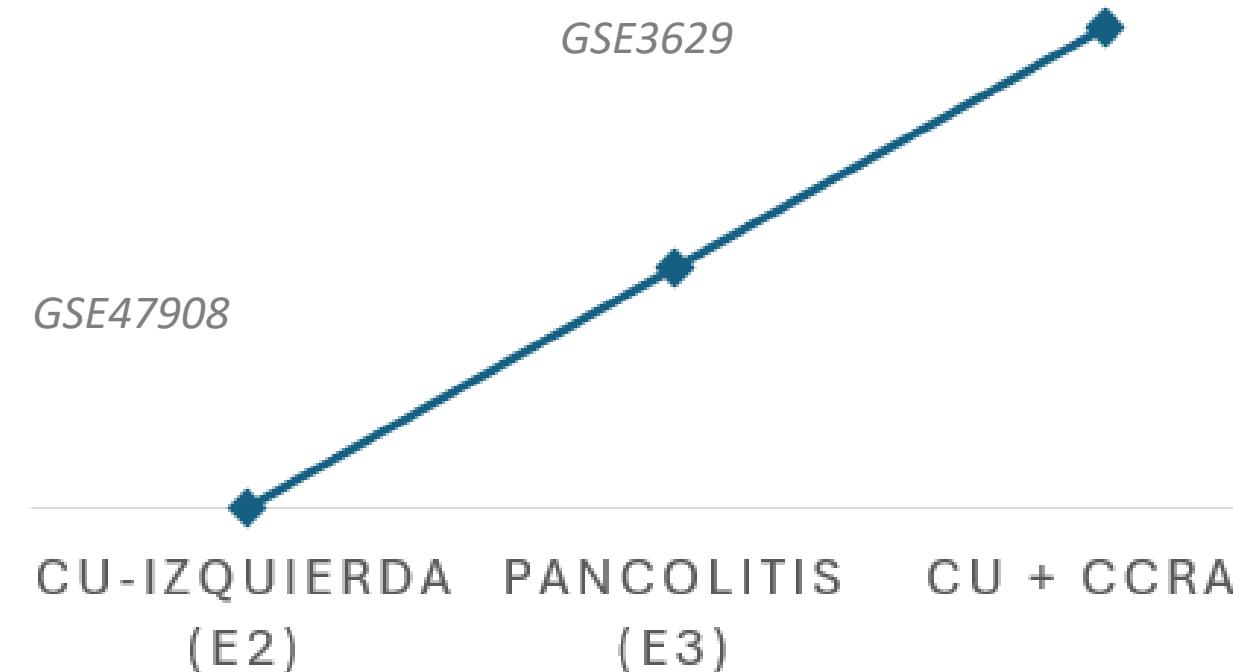
UC AND CACRC / LEFT UC

CU-Left (E2) Pancolitis (E3) CU+ CCRAC

Cumulative Inflammatory Burden (CIM)



↑ CU+CCRAC / CU-I



↓ CU+CCRAC / CU-I

