XIX CONGRESSO NAZIONALE SIES 2026

A Novel Preclinical Mouse Model of Chronic Lymphocytic Leukemia Driven by BCOR Loss in B Cells

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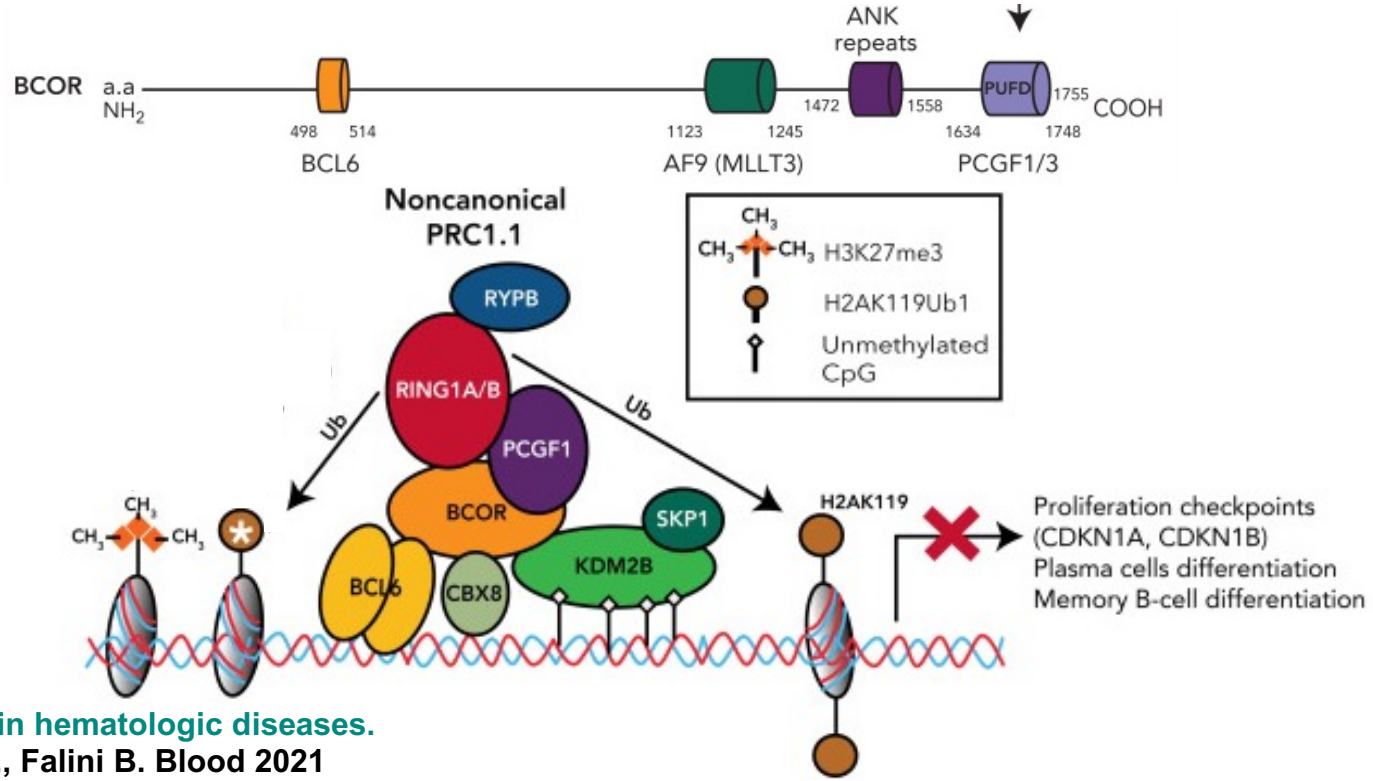
Palazzo degli Affari

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

NOTHING TO DISCLOSE

BCOR is a member of non Canonical Polycomb Repressor Complex (PRC1.1), a repressor complex required for B cell differentiation



BCOR gene alterations in hematologic diseases.
Sportoletti P., Sorcini D., Falini B. Blood 2021

BCOR mutations in CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

- Around 2% in CLL with unmutated IGHV, trisomy 12, and NOTCH1 mutations
- 9% of Asiatic people
- *BCOR* mutations are scattered across the whole length of coding sequence (>exon 4)

- Disruptive inducing premature STOP codons
- Predicted to trigger nonsense mediated mRNA decay

  - reduced *BCOR* mRNA levels
  - absence of full-length BCOR protein
  - lack or low expression of truncated BCOR protein

characteristics of loss-of-function mutations in a tumor suppressor gene

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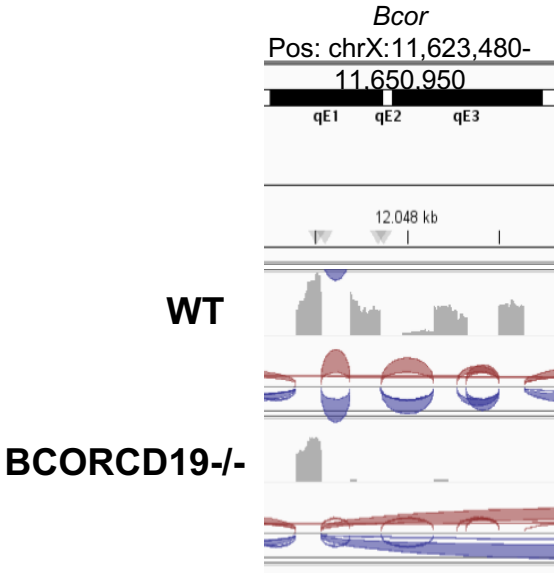
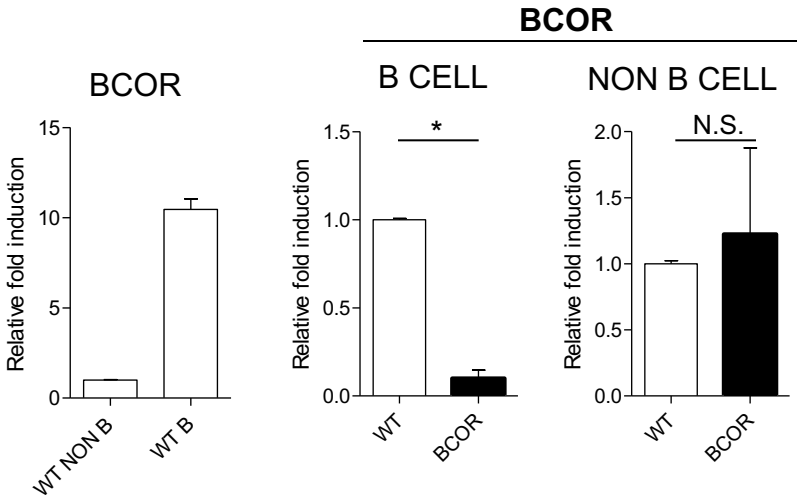
Bcor loss in B cell of mutant mice

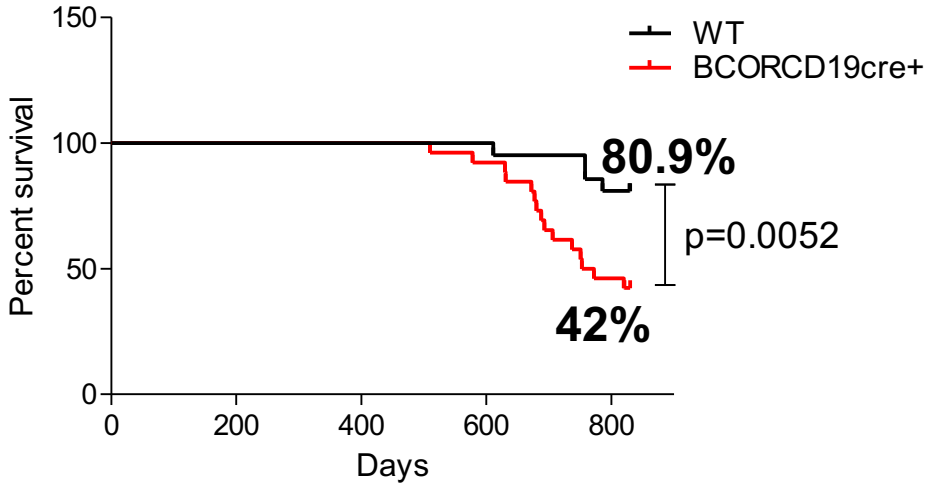
*Bcor f/f × CD19Cre+





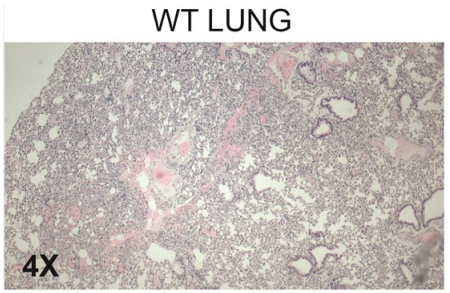
*BCOR loss enhances NOTCH1 in the TCL1 mouse model to promote Richter Transformation
(Rompietti et al. Leukemia 2025)

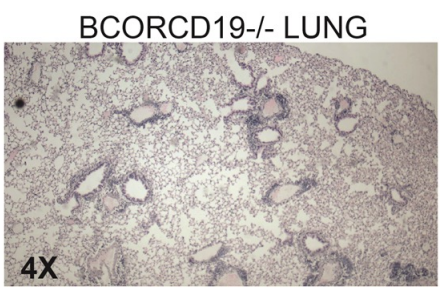
BCORCD19-/- mice exhibit a reduced survival

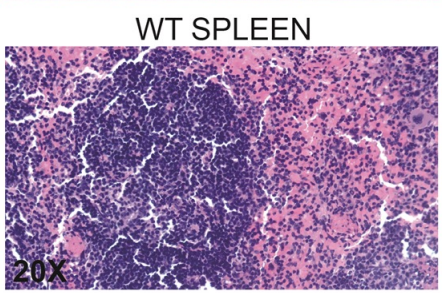


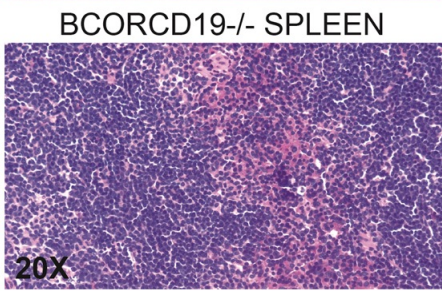
BCORCD19-/- mice median survival 792.5 days, WT mice undefined

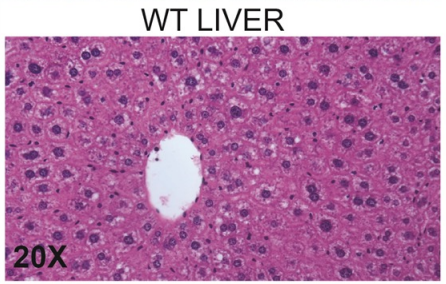
BCORCD19-/- moribund mice show multiple organ infiltration

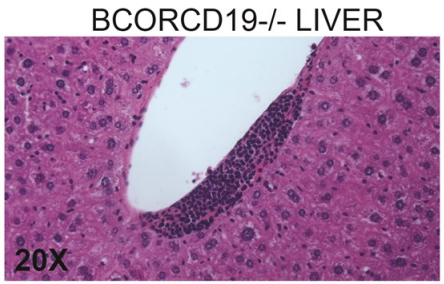


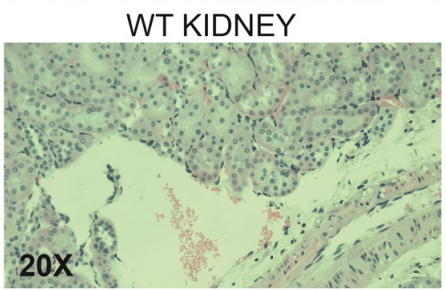


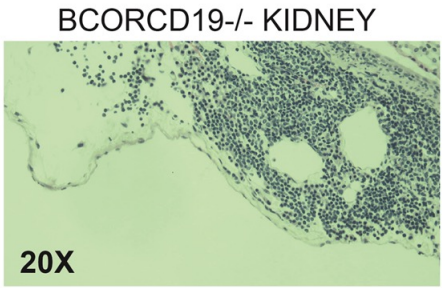




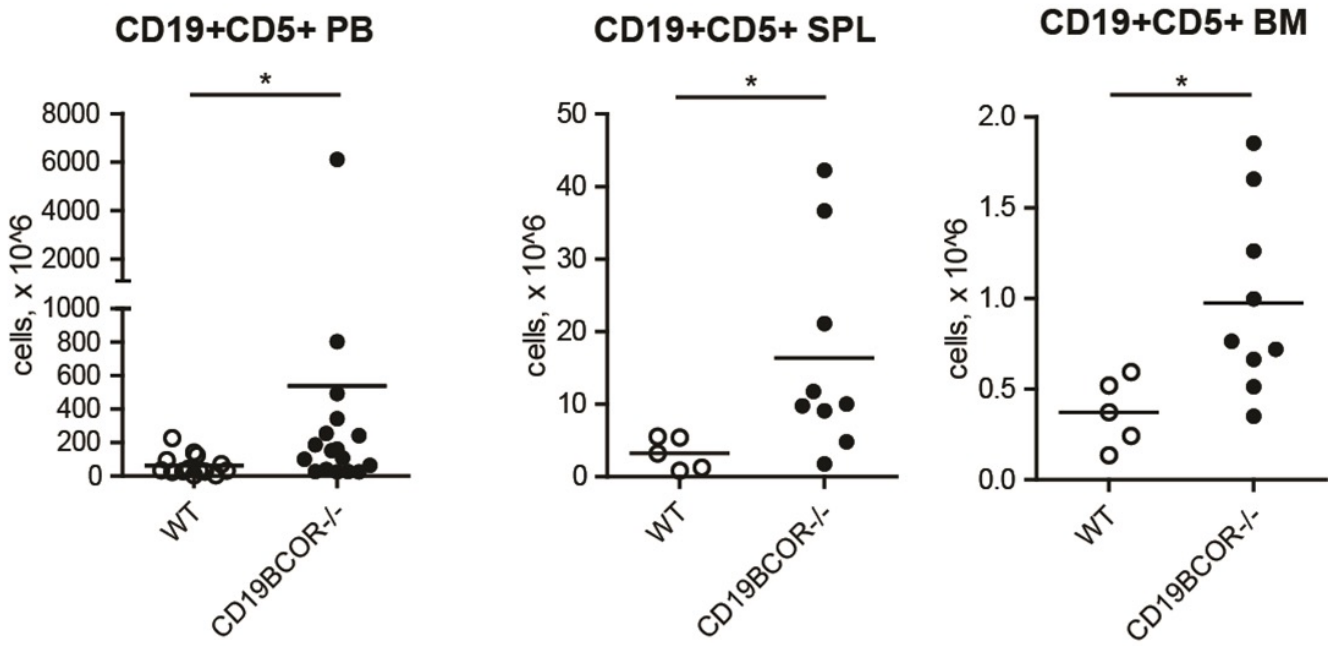




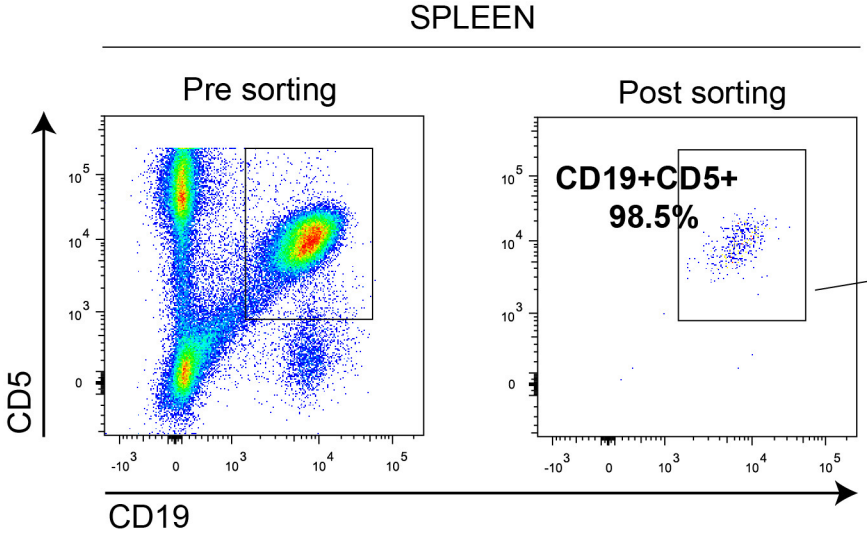




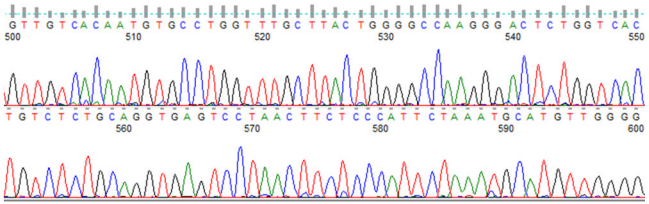
BCORCD19-/- aged mice show an accumulation of leukemic-like B cells CD19+CD5+



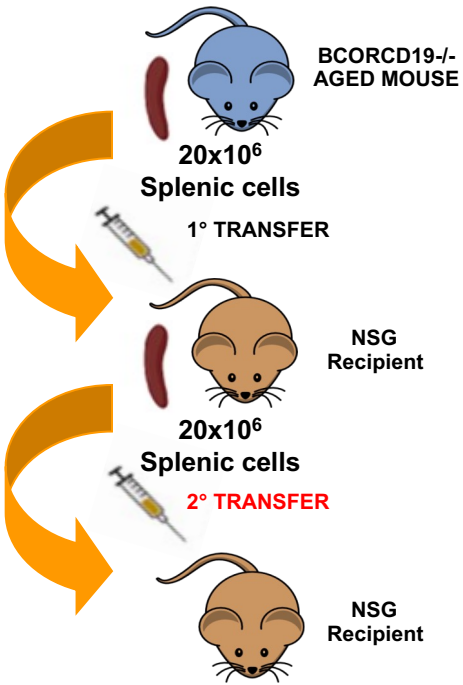
Splenic CD19+CD5+ cells of BCORCD19-/- are monoclonal

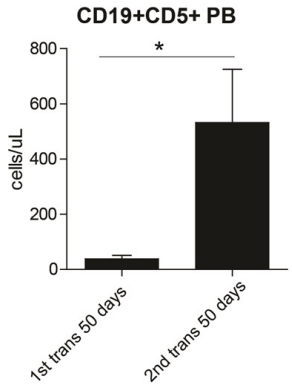


Description	Scientific Name	Total Score	Query Cover	E value	Percent Identy	Accession Length	Accession
Immunoglobulin heavy chain complex (Igh)	Mus musculus strain C57BL/6J chromosome 12, GRCm39	953	100%	0.0	99.81%	120092757	NC_00007 8.7

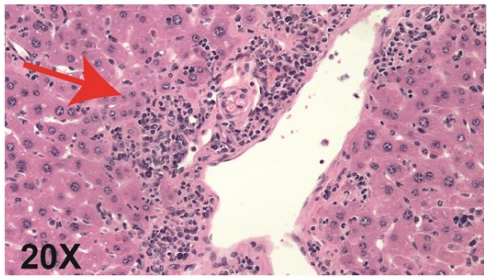


Adoptive transfer of CD19+CD5+ splenic cells from BCORCD19-/- exacerbates disease progression in transplanted mice.

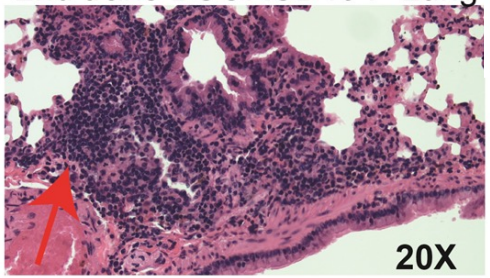




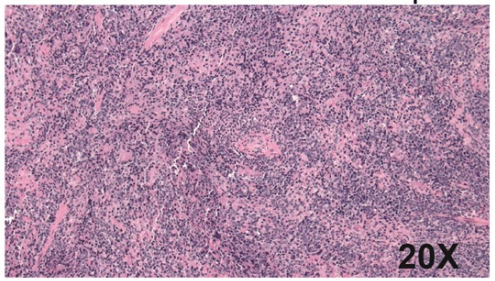
2nd trans BCORCD19-/- Liver



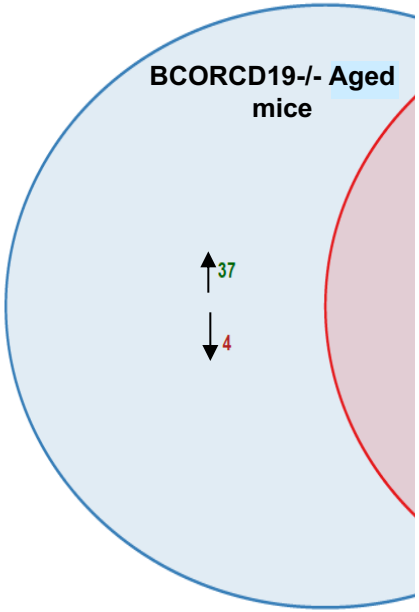
2nd trans BCORCD19-/- Lung

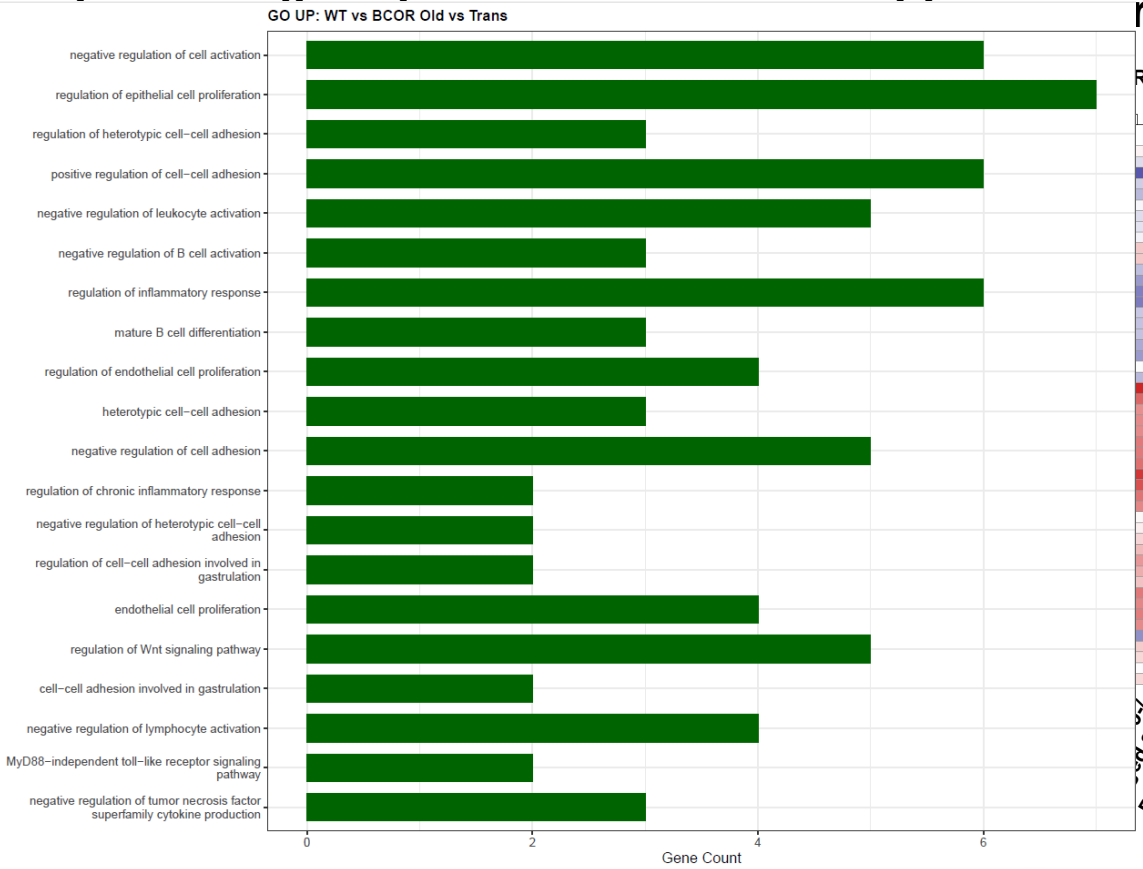


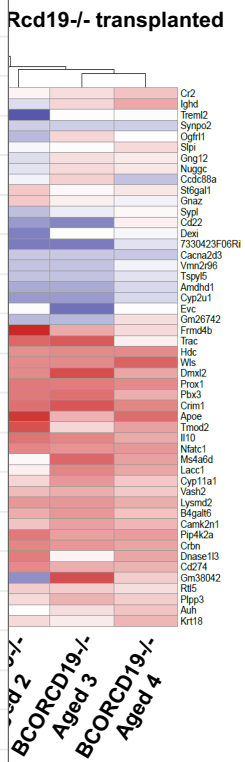
2nd trans BCORCD19-/- Spleen



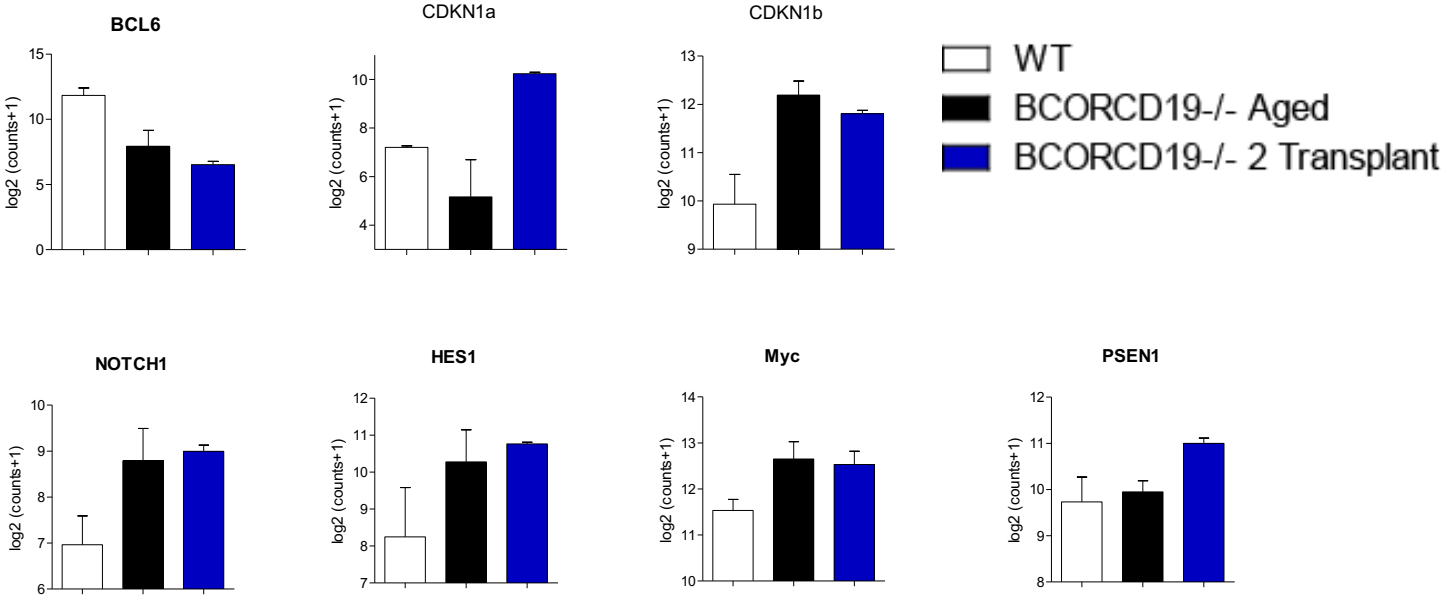
BCORCD19-/- mic red to WT



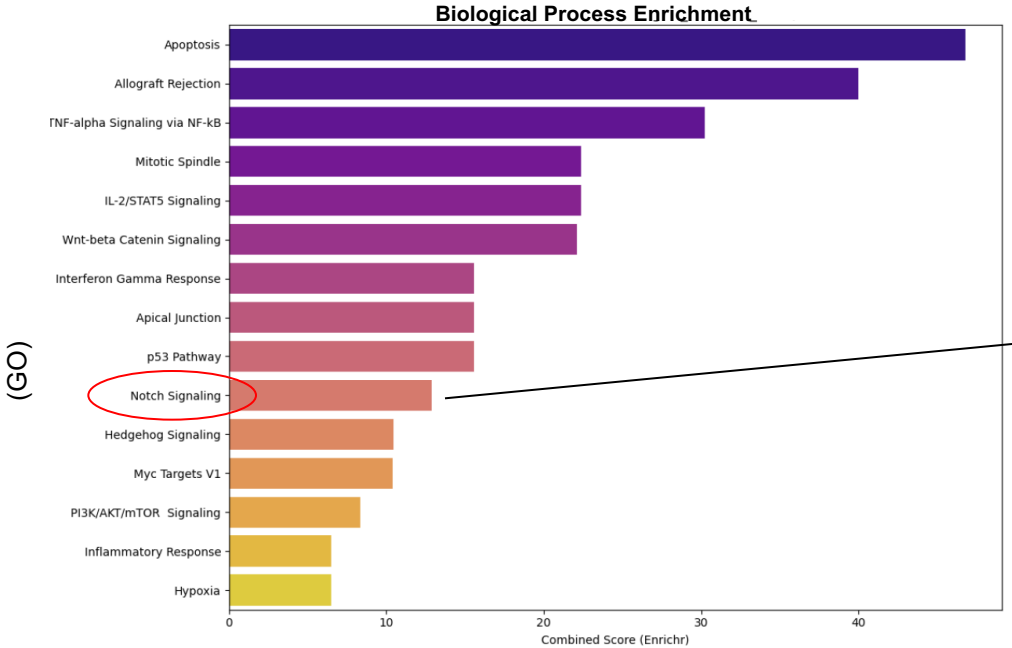


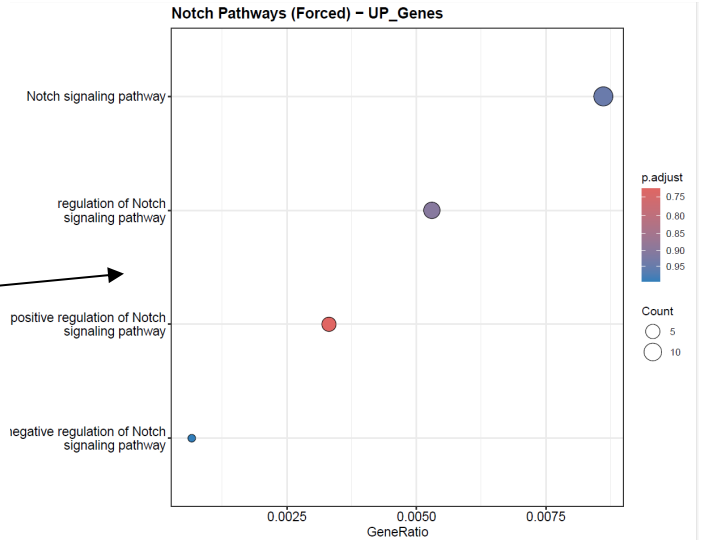


BCORCD19-/- mice show a deregulation on PRC1.1 targets and on NOTCH1 pathway



Enrichment for *notch1* pathway genes is present in human and mouse BCOR-/- CLL





CONCLUSION

•BCOR loss in B cell promote a late onset CLL in mice

•NOTCH1 pathway deregulation is an event that perturbs B cell in the absence of BCOR

•BCOR-/- murine CLL resembles the molecular features of human BCOR-mutant CLL

•BCORCD19-/- mice represent a novel preclinical model of CLL and a valid platform to test new specific target drugs;

GRAZIE A TUTTI PER L'ATTENZIONE

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