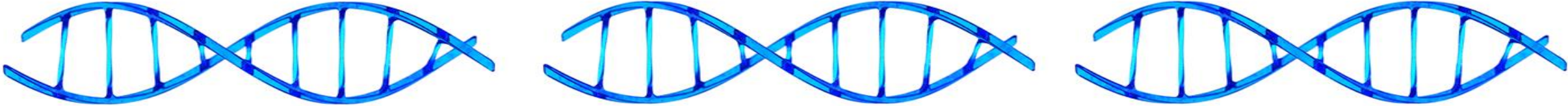
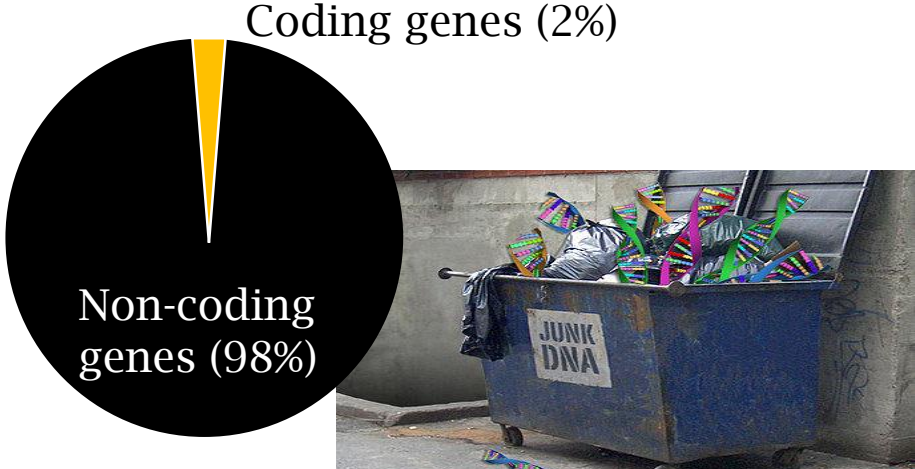


Non-coding RNAs in Erdheim-Chester Disease

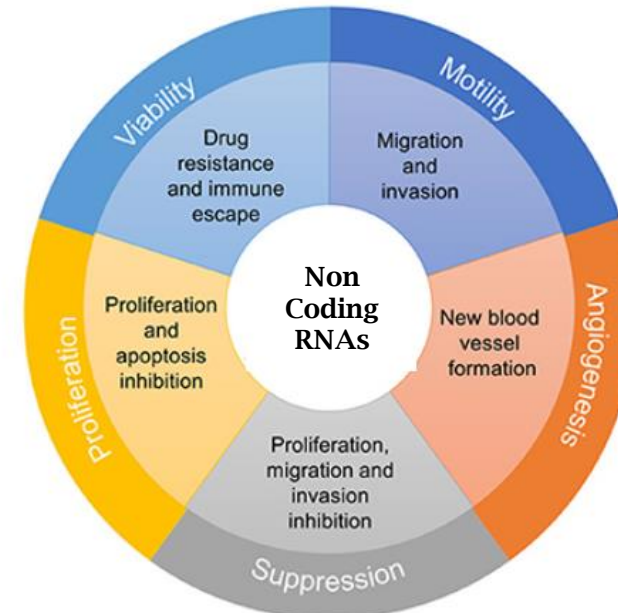
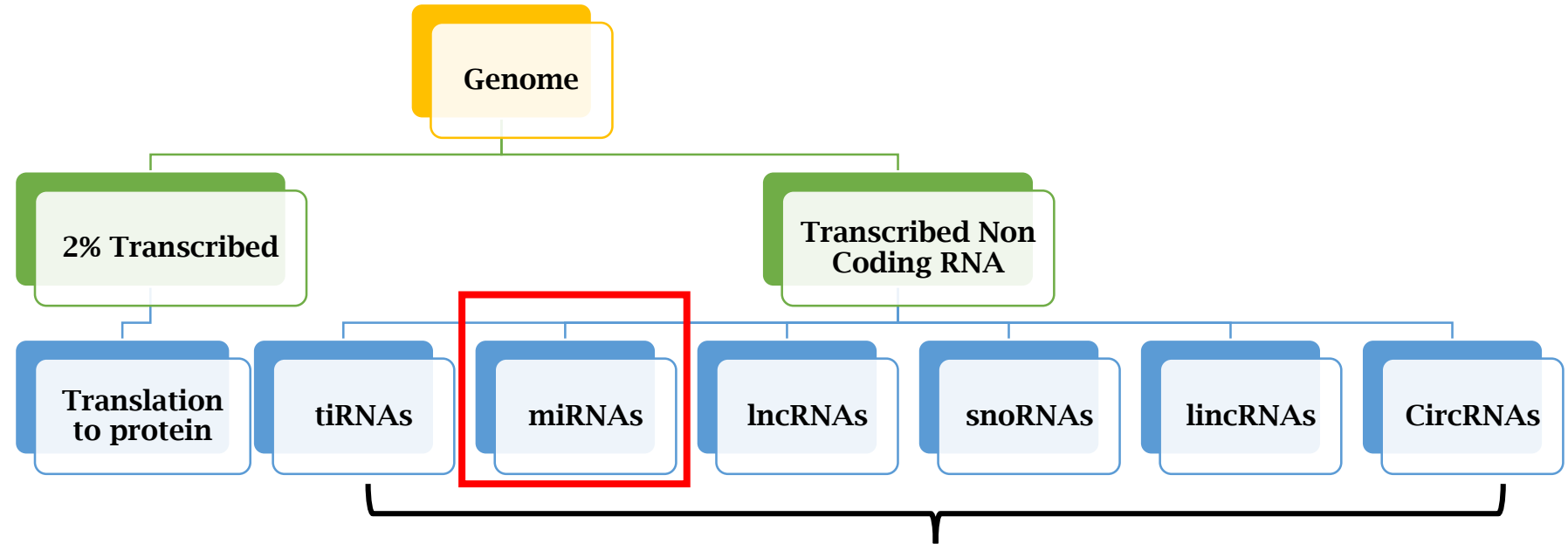


Oshrat Rokah, PhD
November 16th, 2021

The Human Genome



The hidden power of "junk DNA"

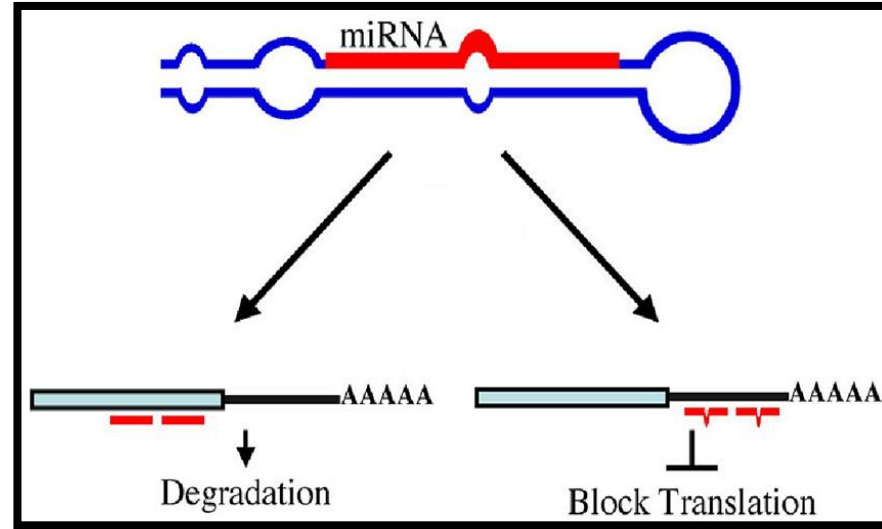


MicroRNAs can be used as...

Biomarkers



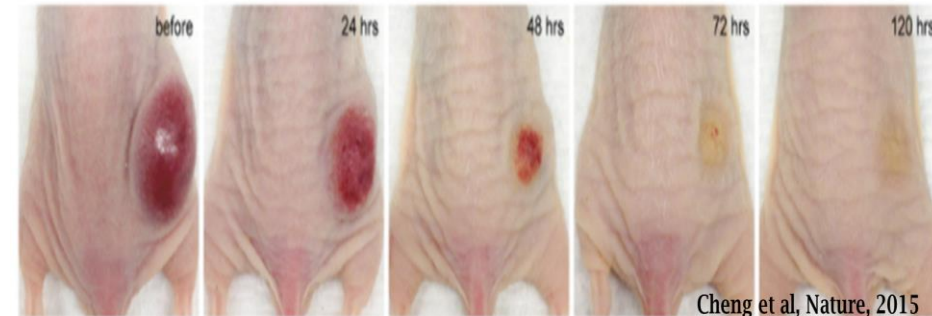
Post-transcriptional regulators



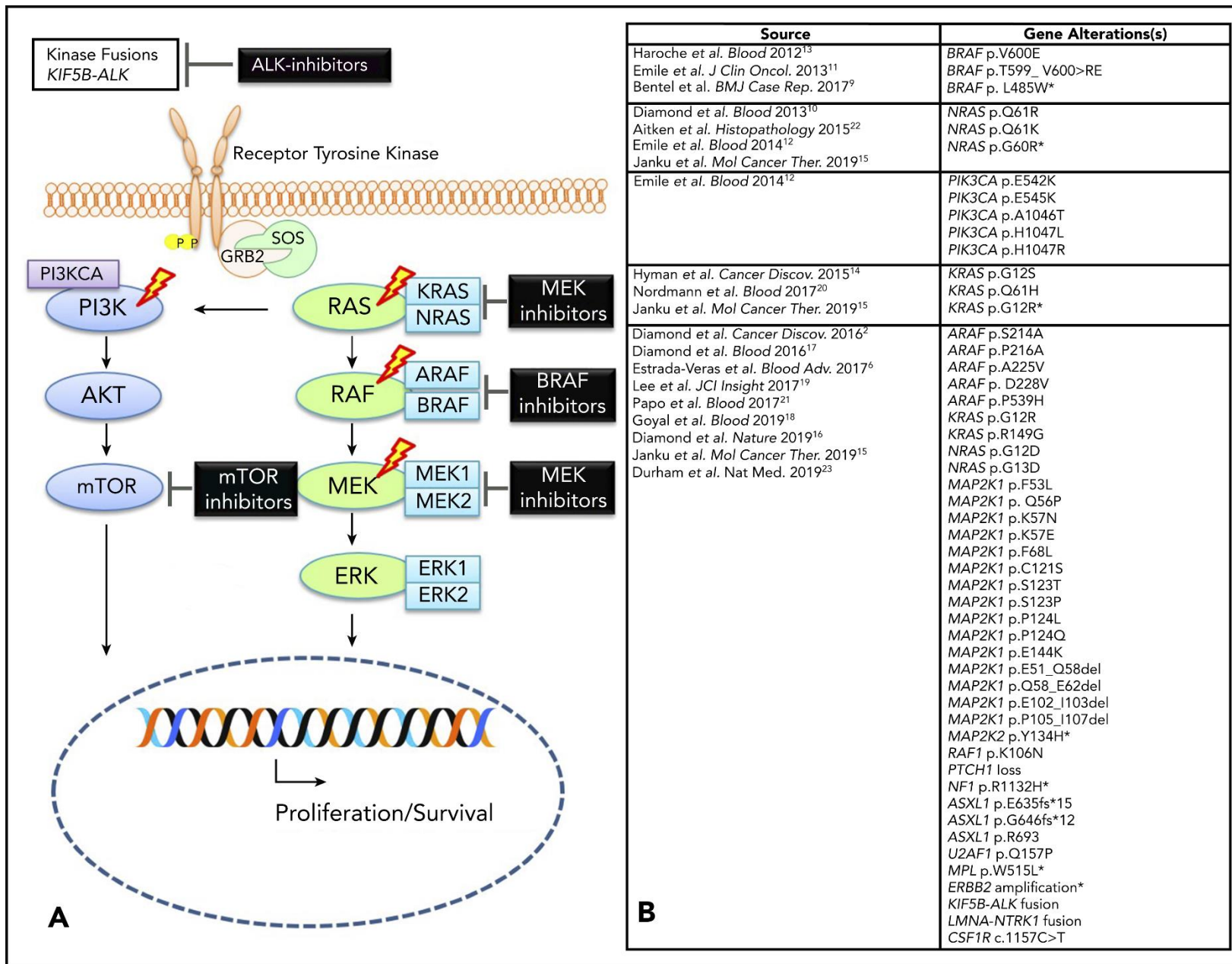
Therapeutic targets



- ~2600 in human genome
- Highly stable in clinical samples
- Expressed in a variety of body fluids
- Phylogenetically conserved
- Differentially expressed

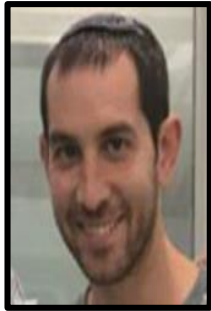


Aggressive Lymphoma mouse model treated with miR-155 inhibitor



Goyal et al, Blood, 2020

Our patients



Ran Weissman,
PhD student

As you start and end your day, say **THANK YOU**
for every little things in your life. And you
will come to realize how blessed you truly
are.

Vergi Crush



Our collaborators



- Eli Diamond
- Omar Abdel-Wahab
- Benjamin Durham

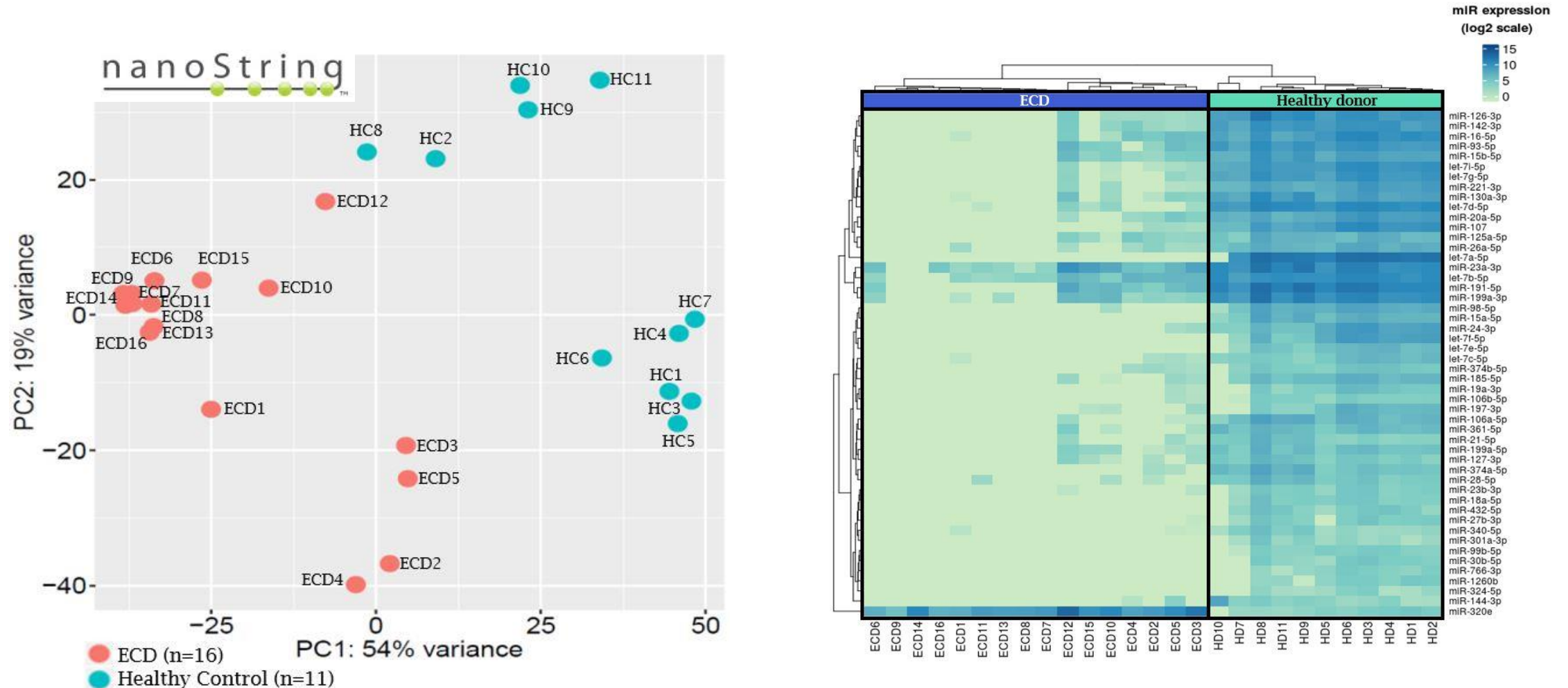


- Julien Haroche
- Jean-François Emile

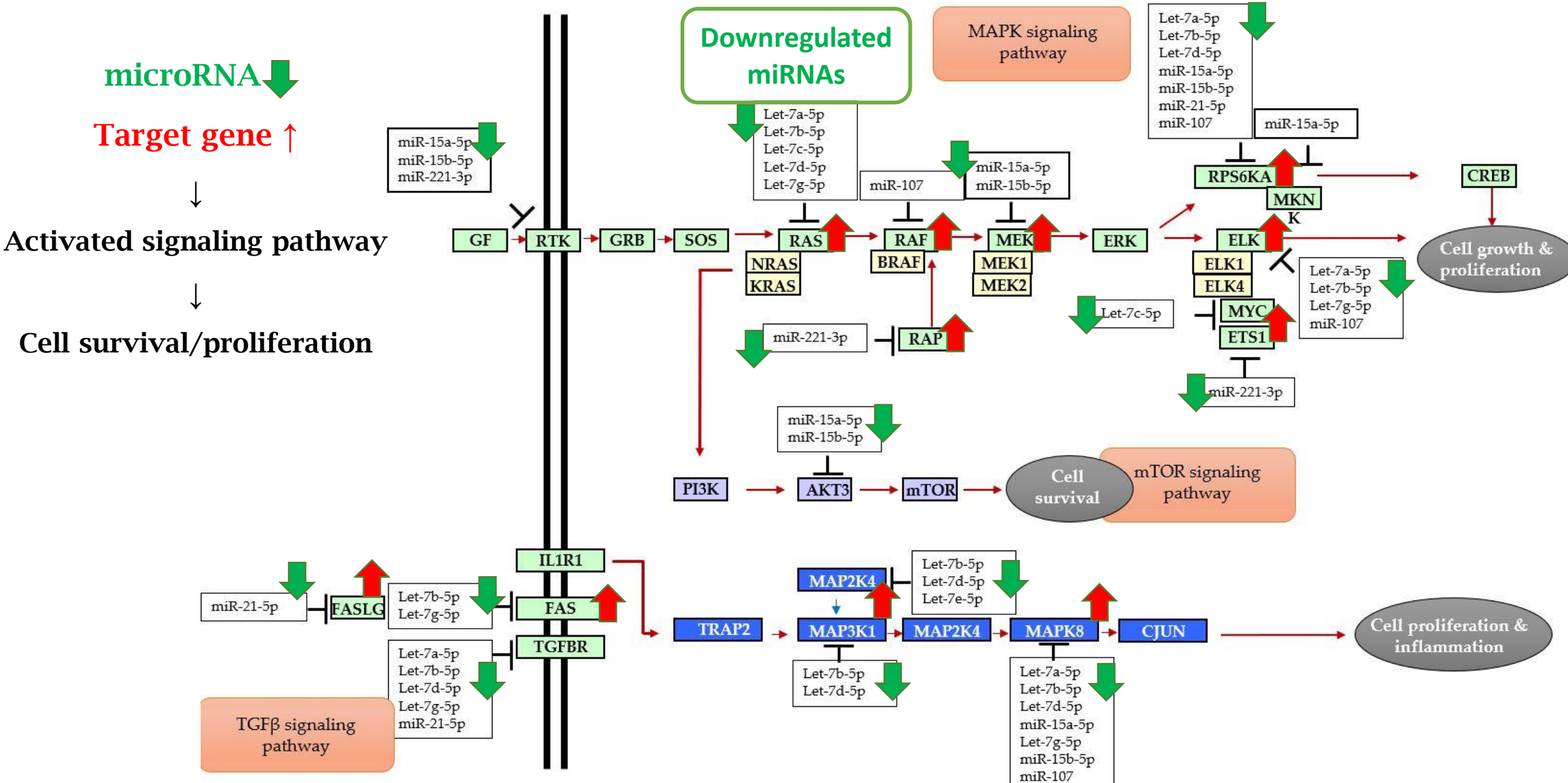


- Noam Shomron

MiRNA expression patterns in ECD patients compared with healthy individuals

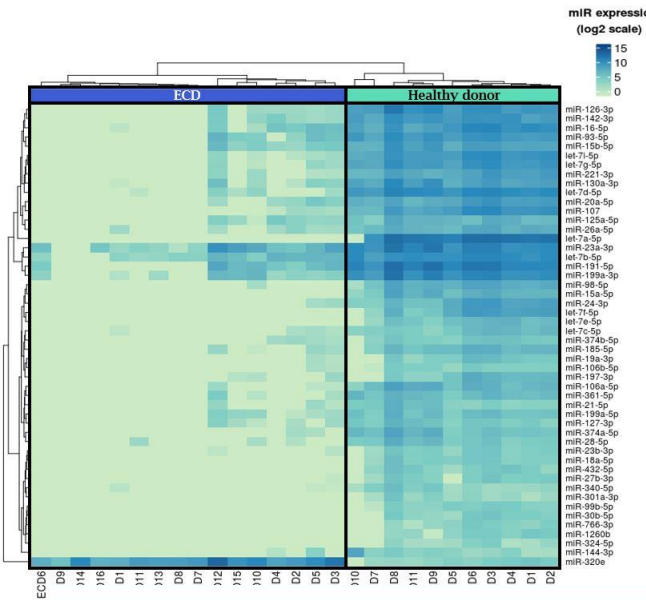


Differential microRNA expression in plasma samples of ECD patients and healthy controls

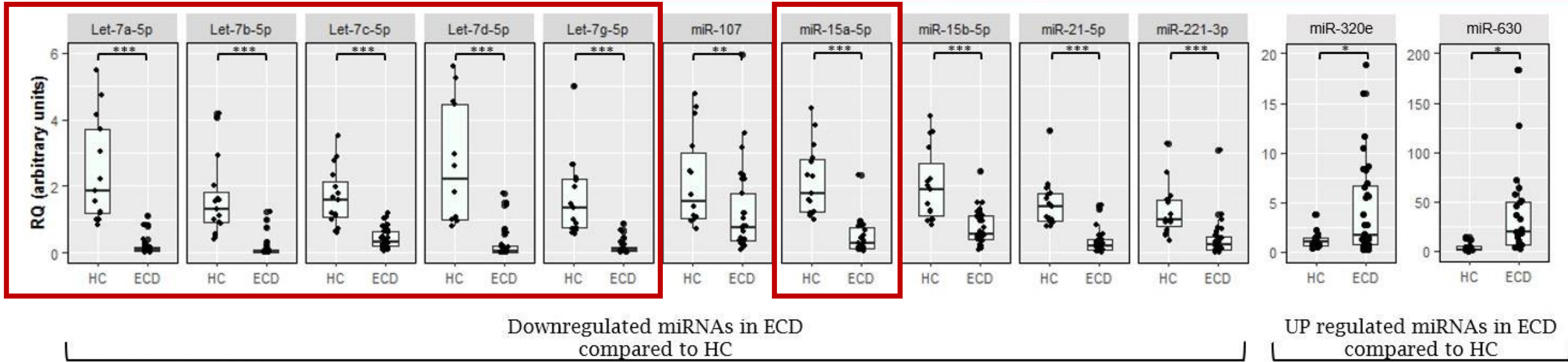


Weissman & Diamond et. al., Cancers, 2020

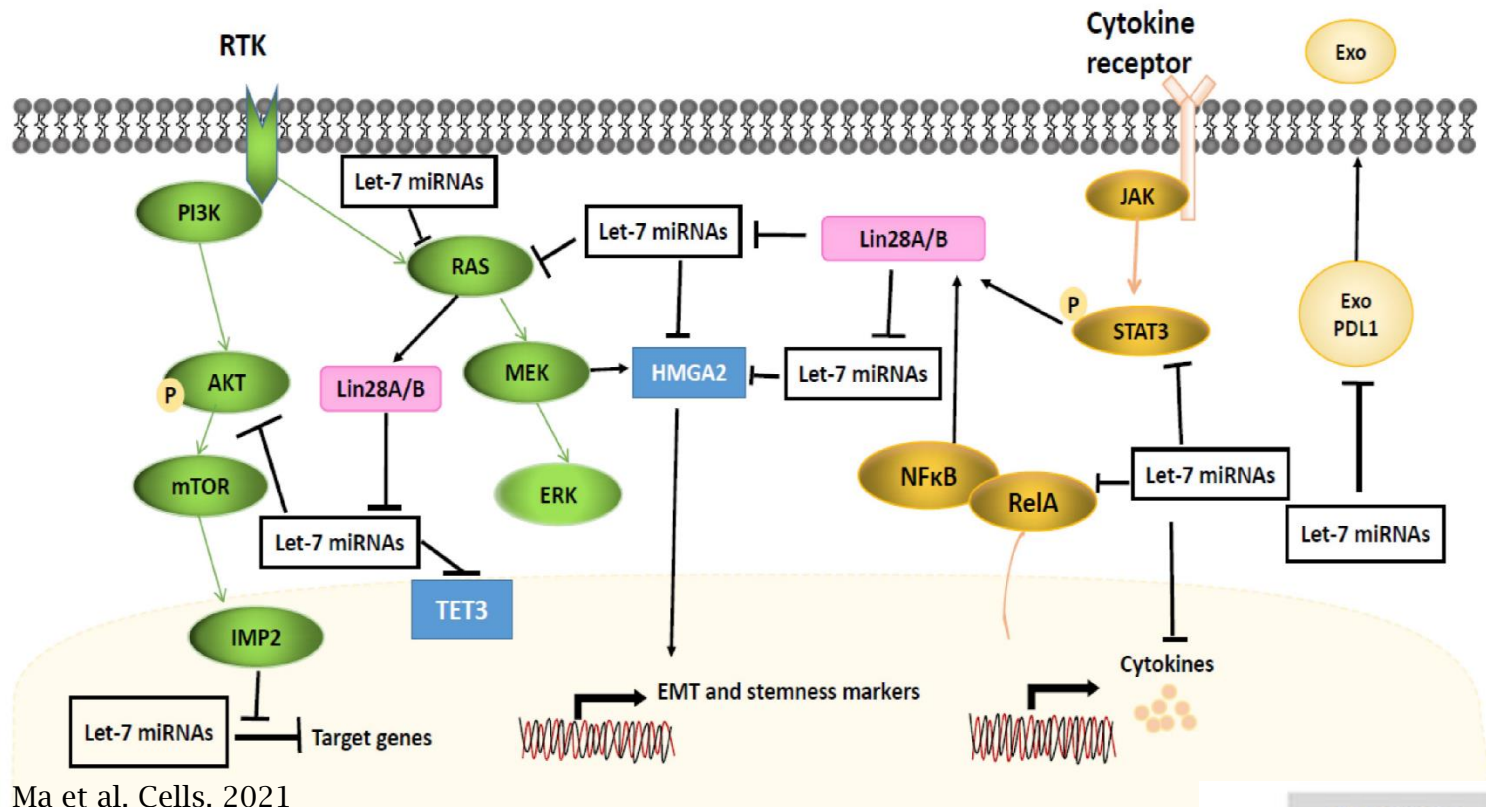
Validation of miRNAs expression in plasma samples of ECD patients and healthy controls



Real Time-PCR validation [ECD n=32, HC n=15]

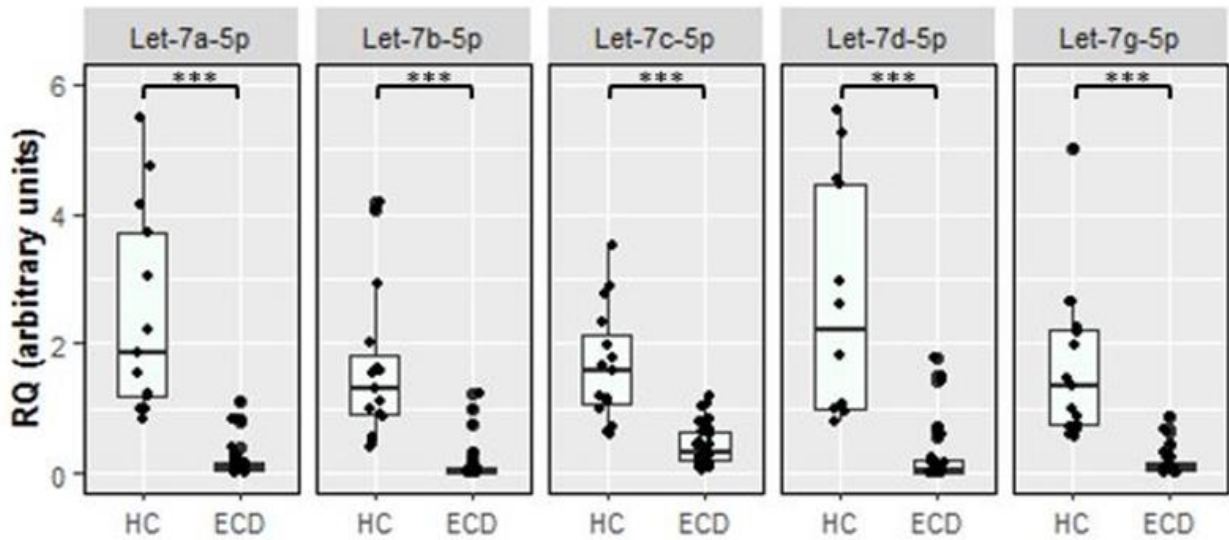
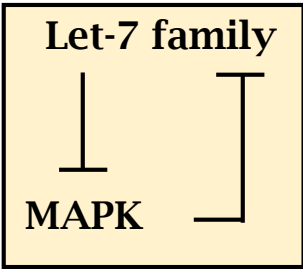


*p<0.05, **p<0.01, ***p<0.001



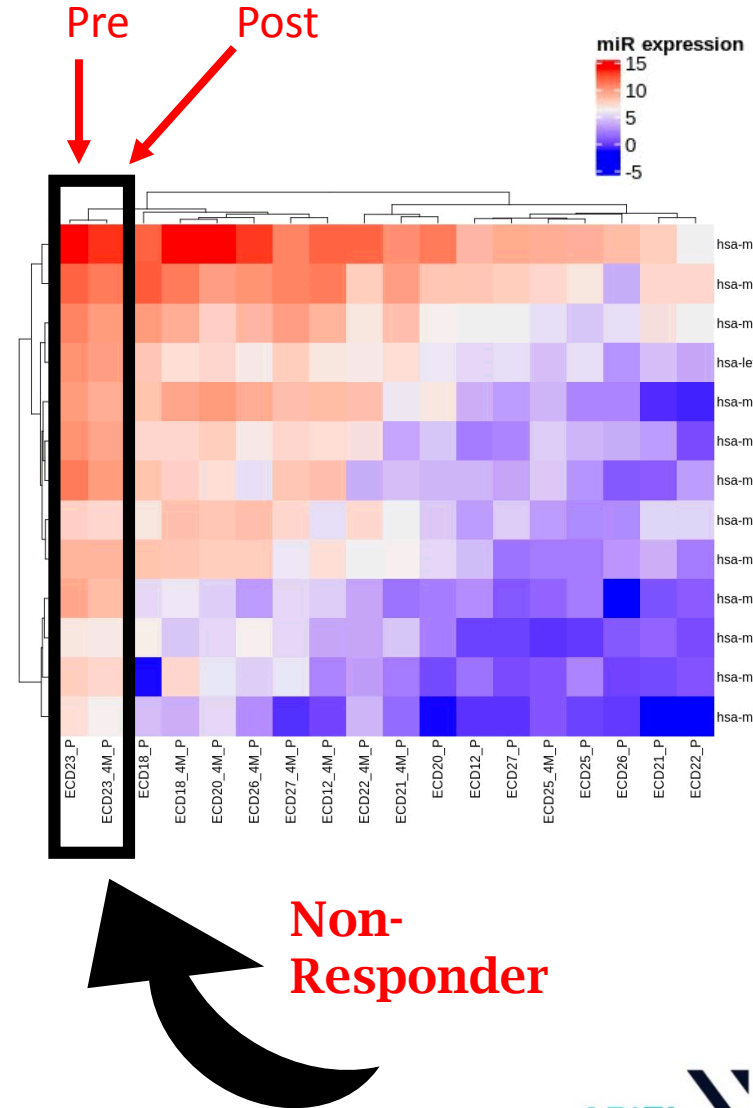
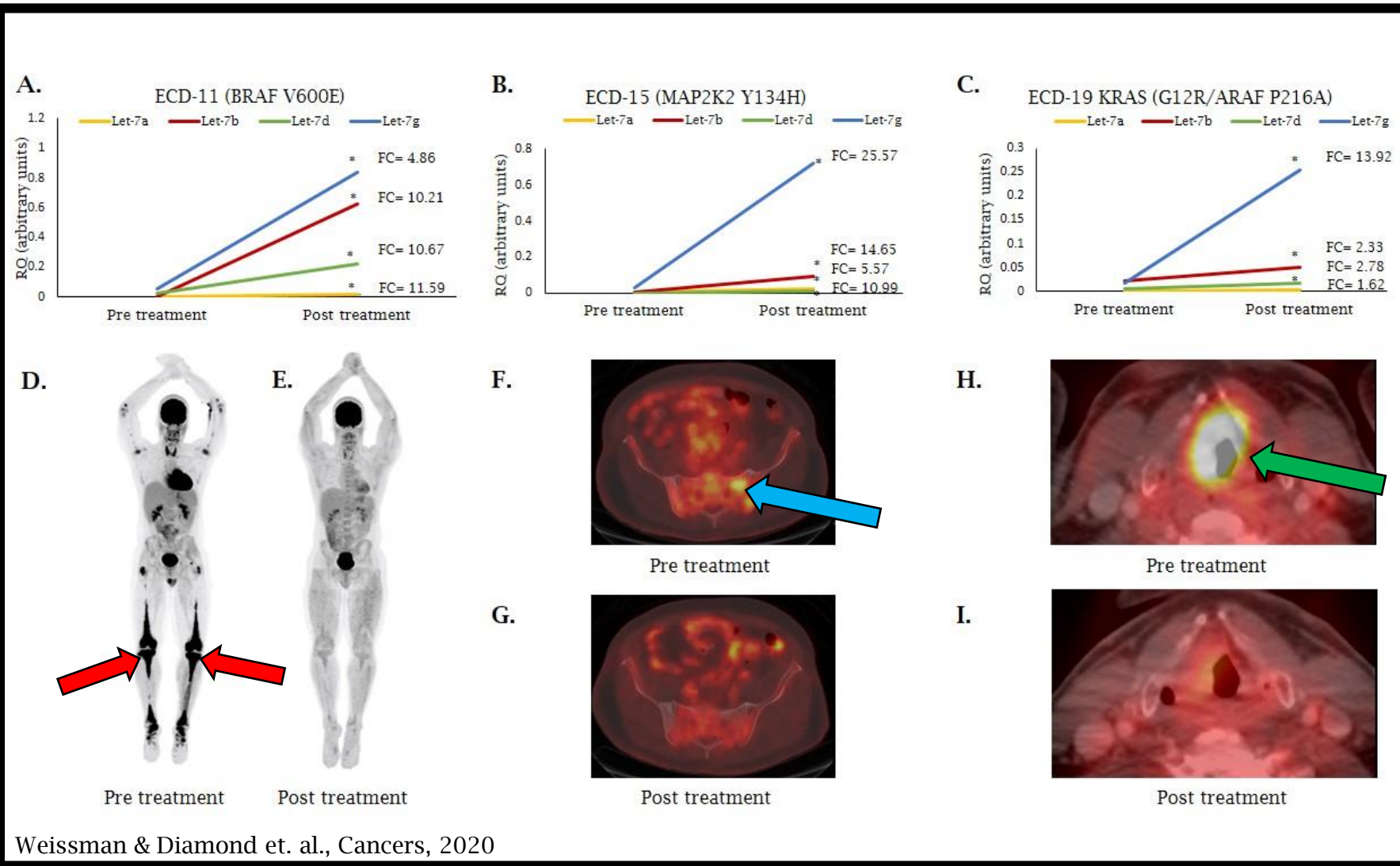
Ma et al. Cells, 2021

The let-7 family is considered as tumor suppressor miRNAs since they regulate oncogenic pathways in numerous types of tumors



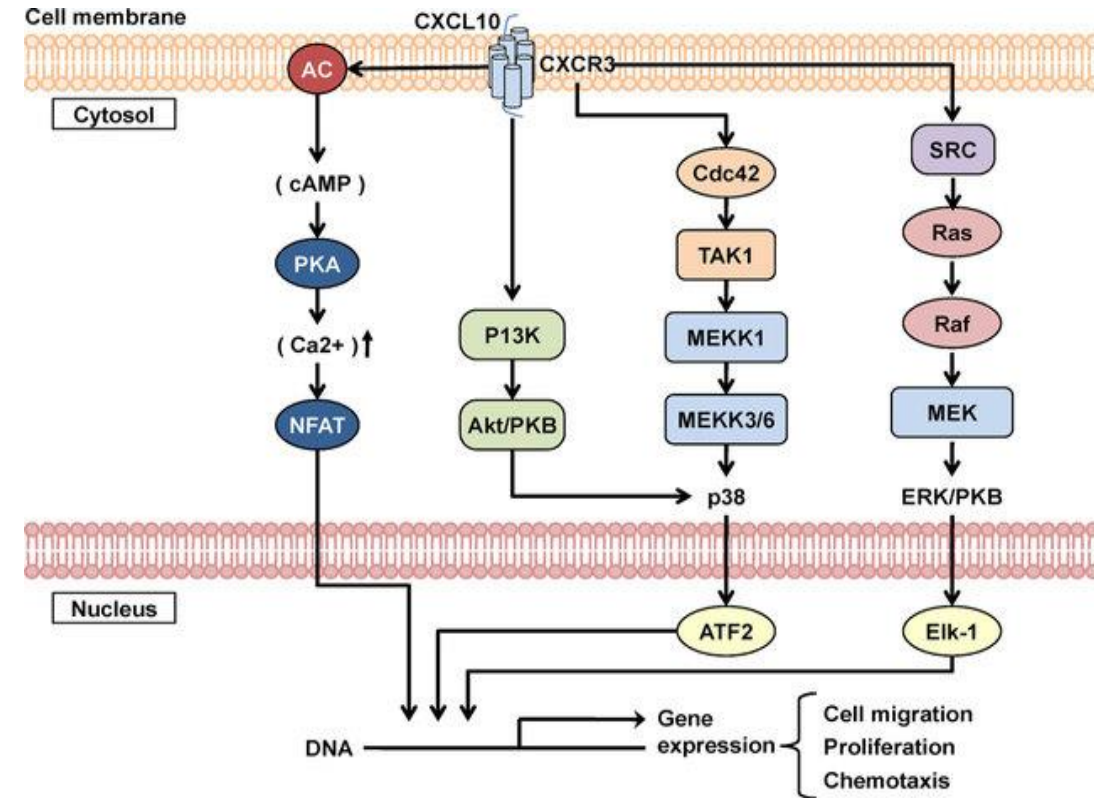
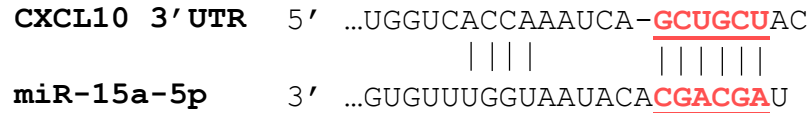
Weissman & Diamond et. al., Cancers, 2020

MicroRNA expression following ERK Signaling Cascade Inhibition

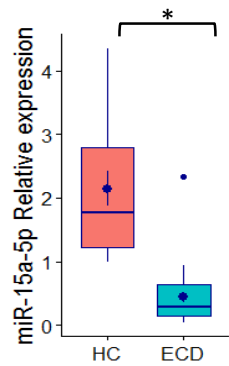


Weissman & Diamond et. al., Cancers, 2020

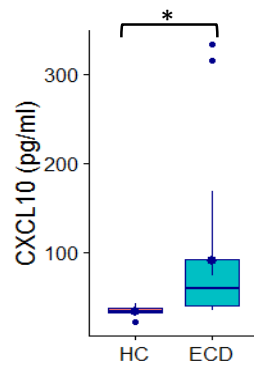
miR-15a-5p regulates CXCL10 expression in ECD patients



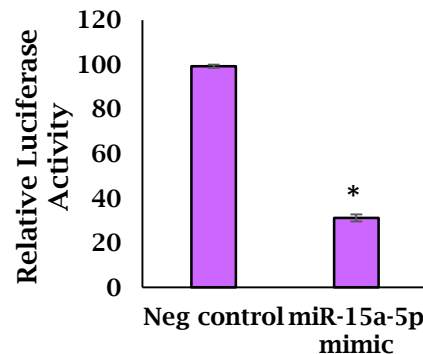
miR-15a-5p levels in plasma samples of ECD and HC



Secreted CXCL10 levels in plasma samples of 24 ECD patients and 10 HC



Luciferase activity



miR-15a-5p
 Downregulated
 in ECD patients

CXCL10
 Upregulated
 in ECD patients

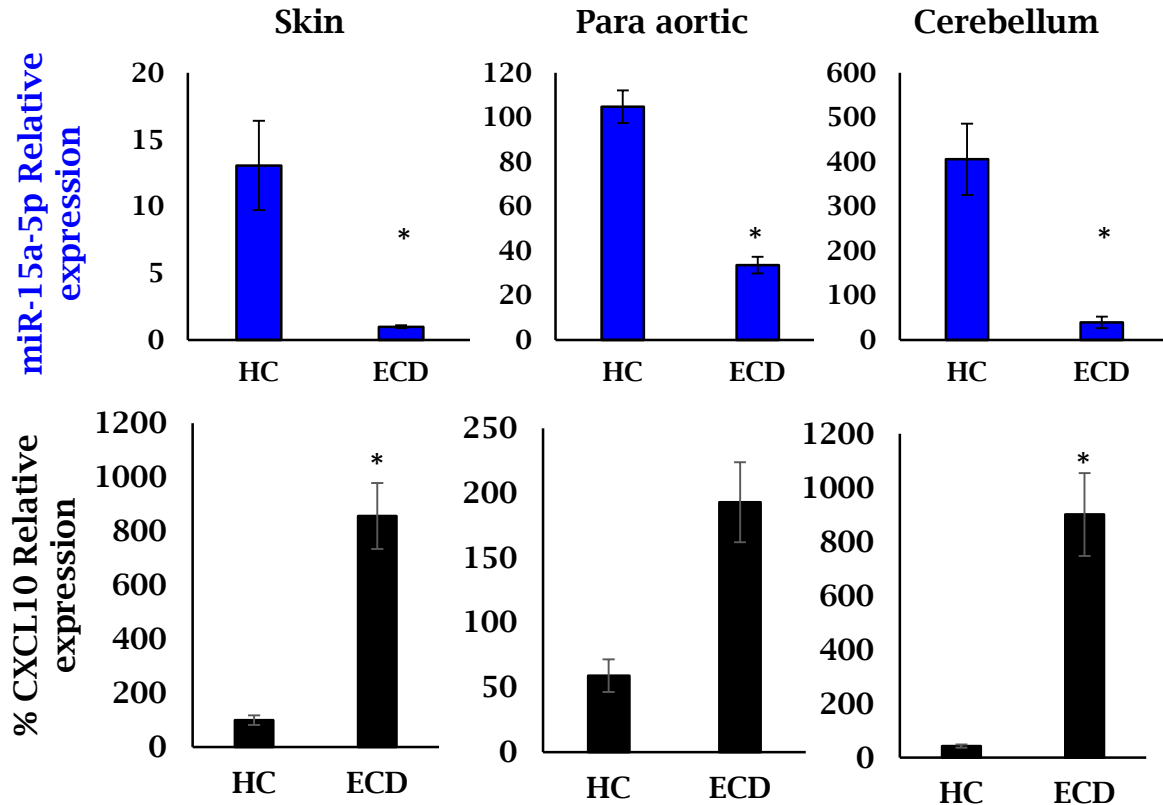
CXCL10 is highly expressed in:

- Inflammatory and autoimmune diseases
- Cancer

miR-15a-5p and CXCL10 expression in tissue biopsies of ECD patients

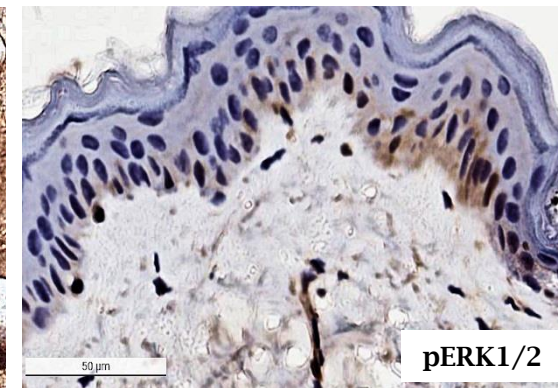
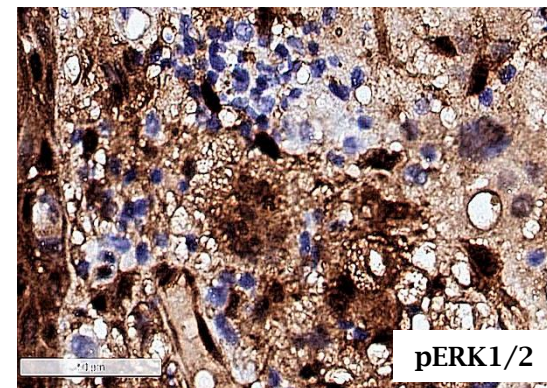
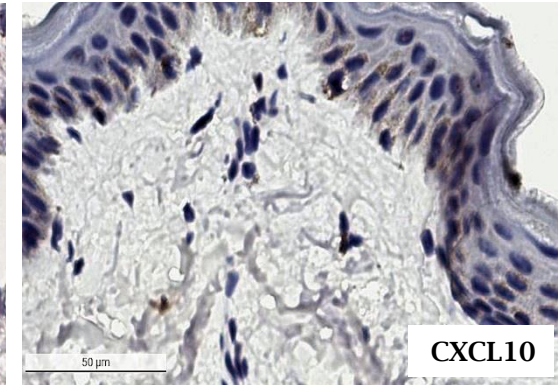
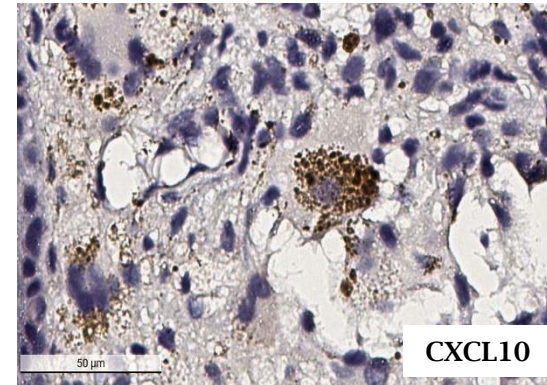
RNA level

Protein level

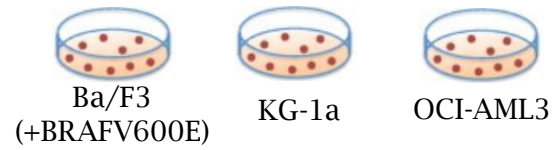


ECD Patient

Non-ECD Control Patient

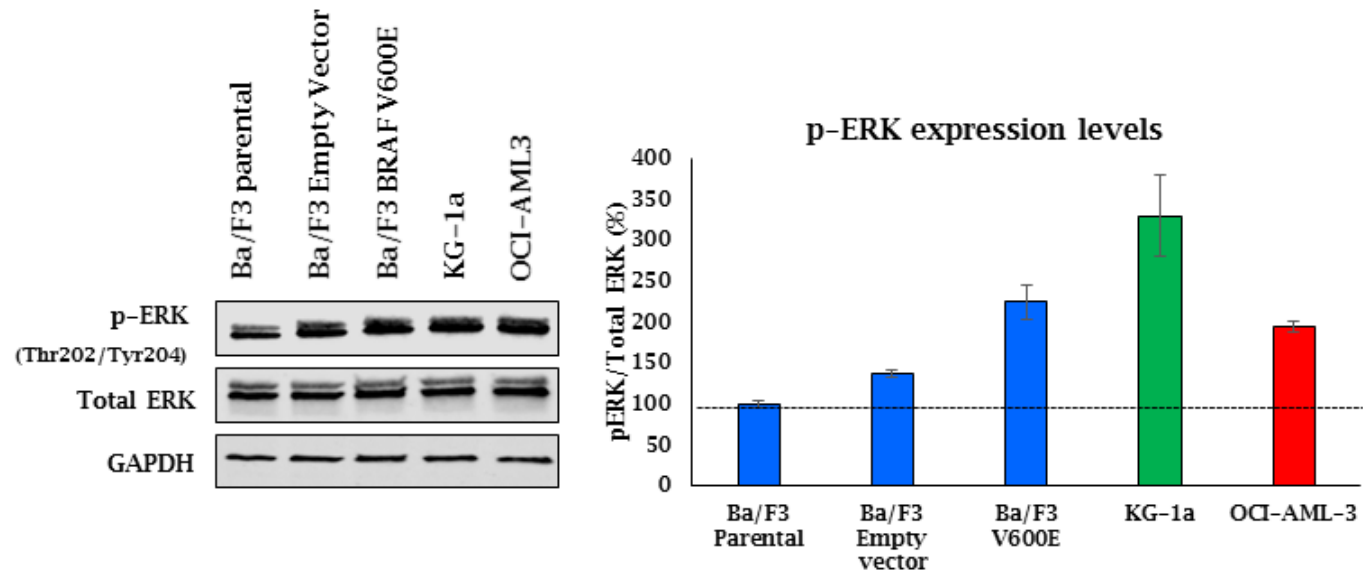


Functional studying of the miR-15a-5p in cells over expressing MAPK pathway

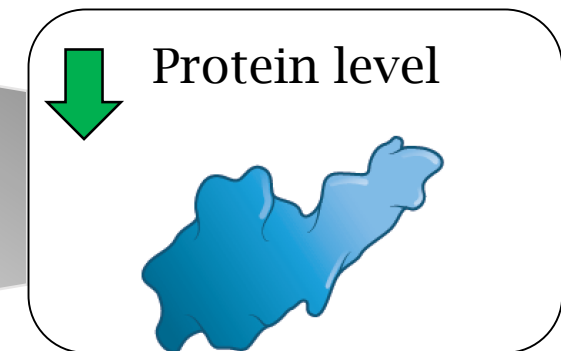
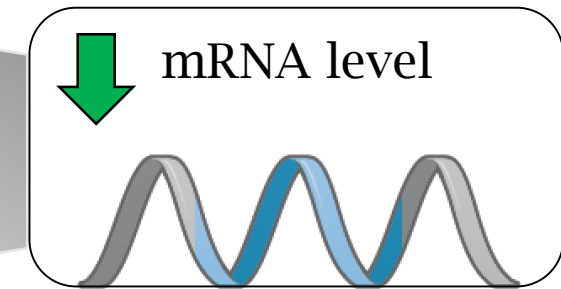
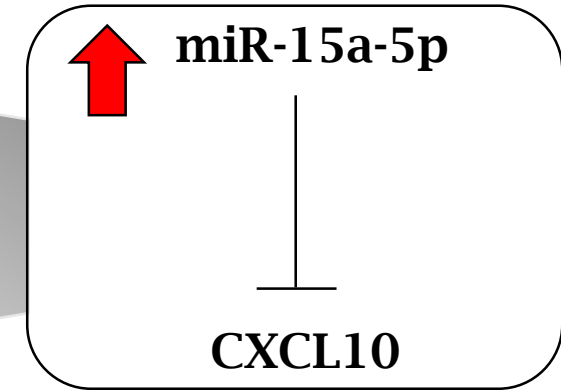
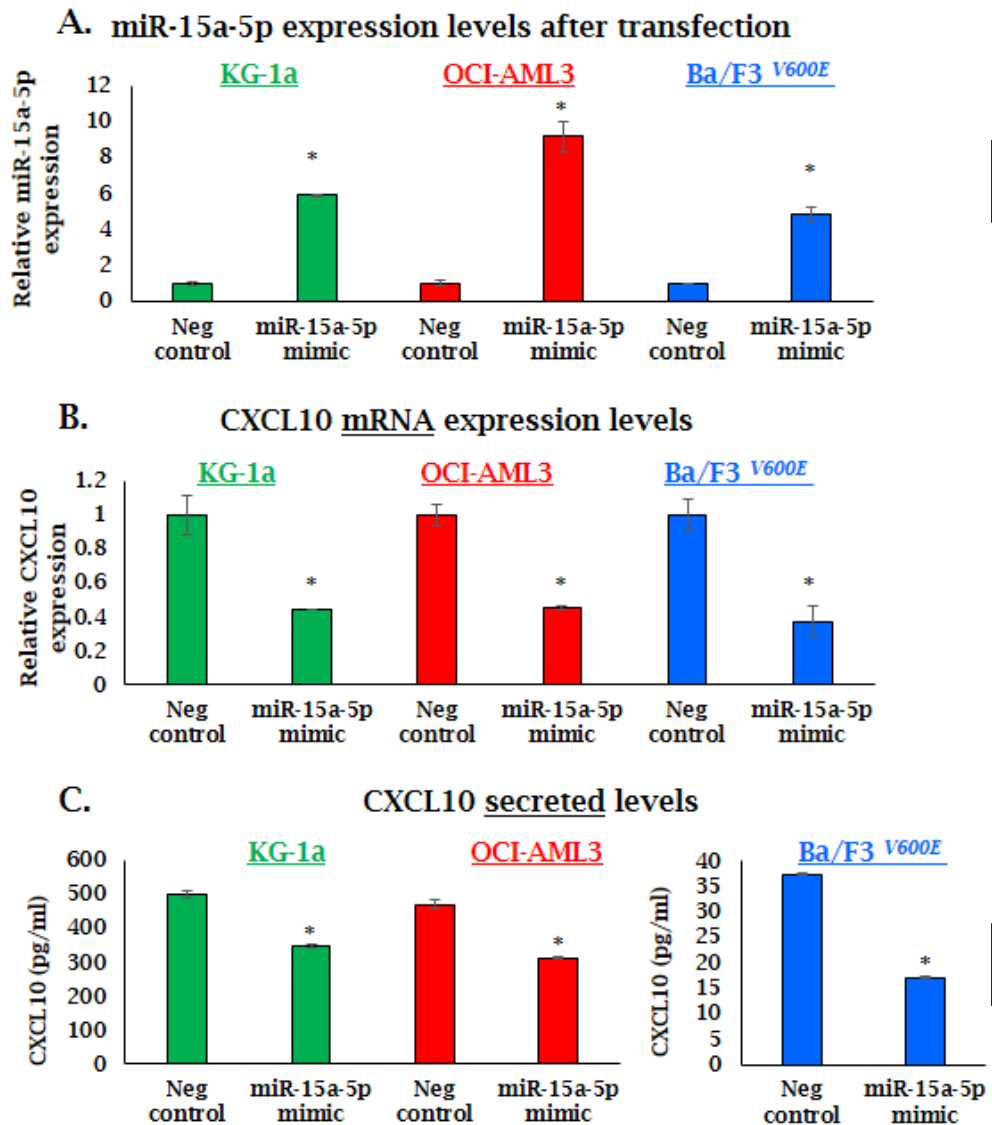


Over-expressing MAPK signaling

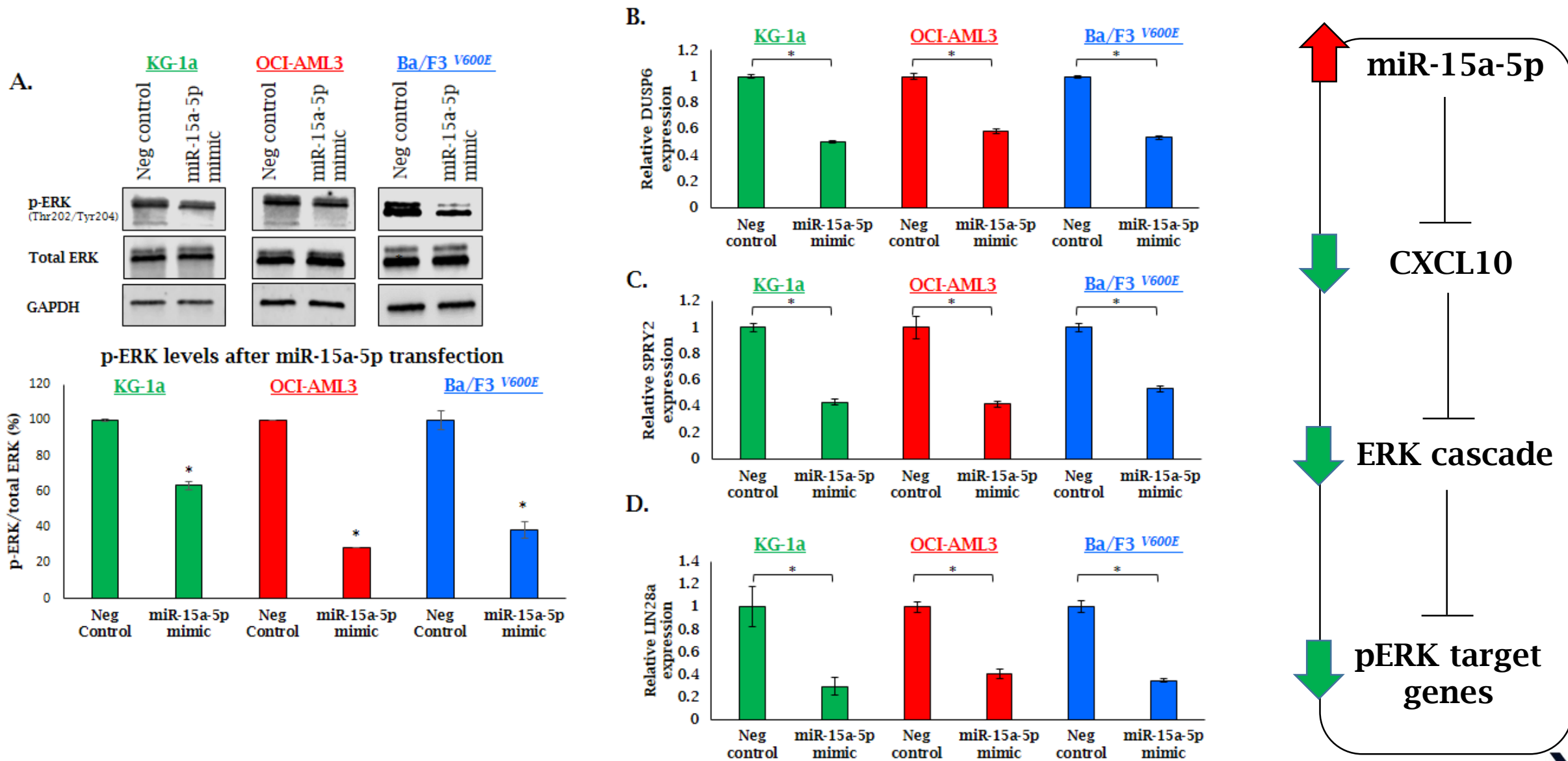
p-ERK protein levels



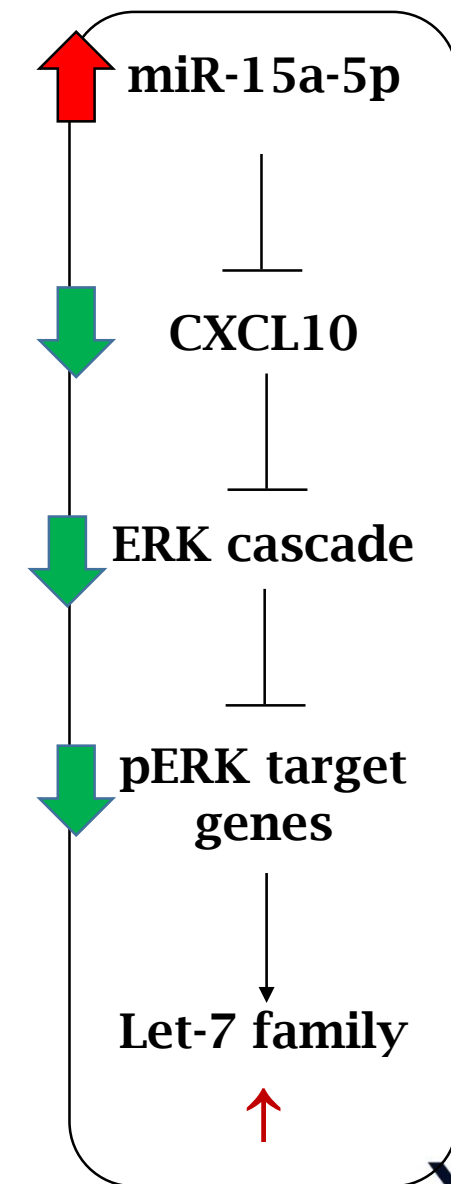
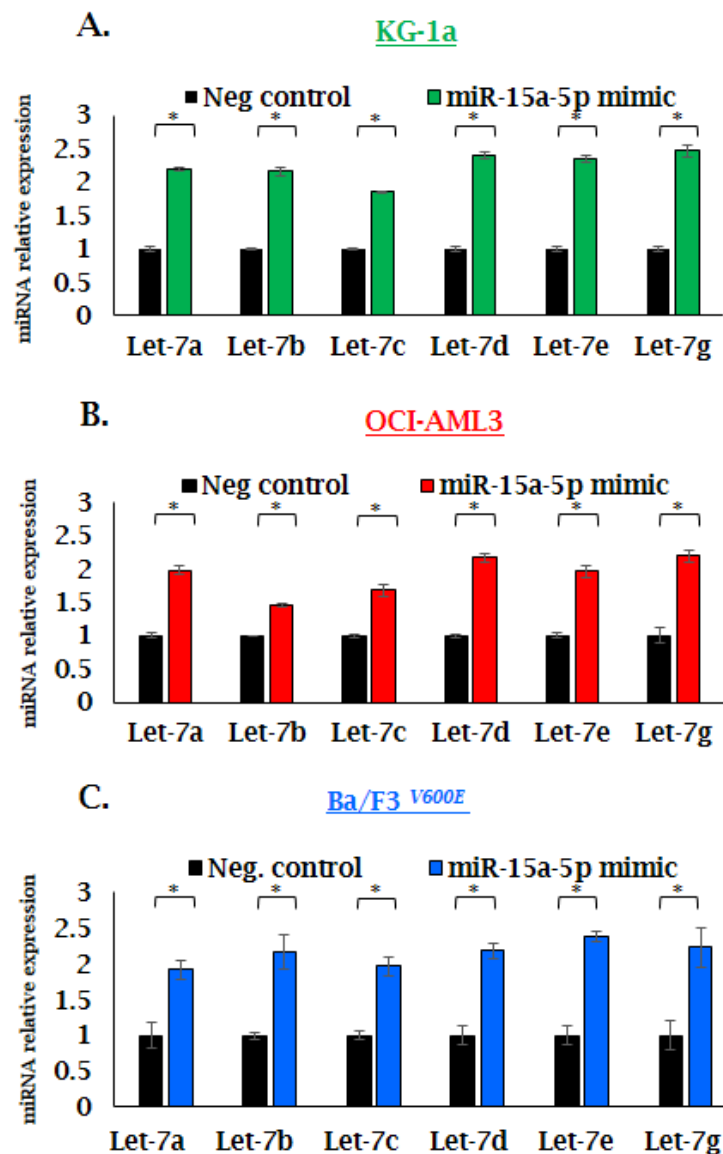
CXCL10 mRNA and protein levels after miR-15a-5p mimic transfection



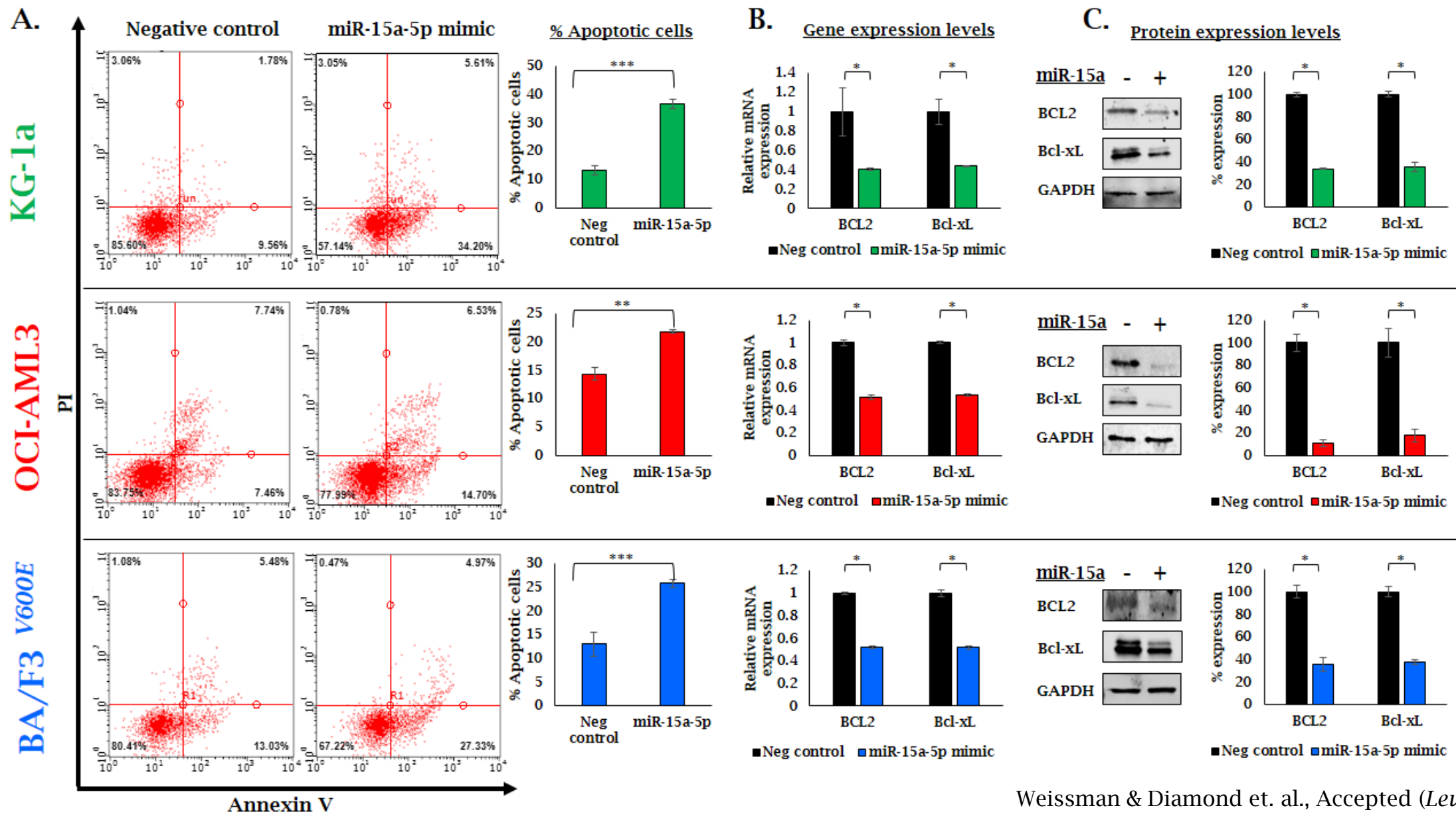
Low expression of CXCL10 results in downregulation of p-ERK signaling and target genes



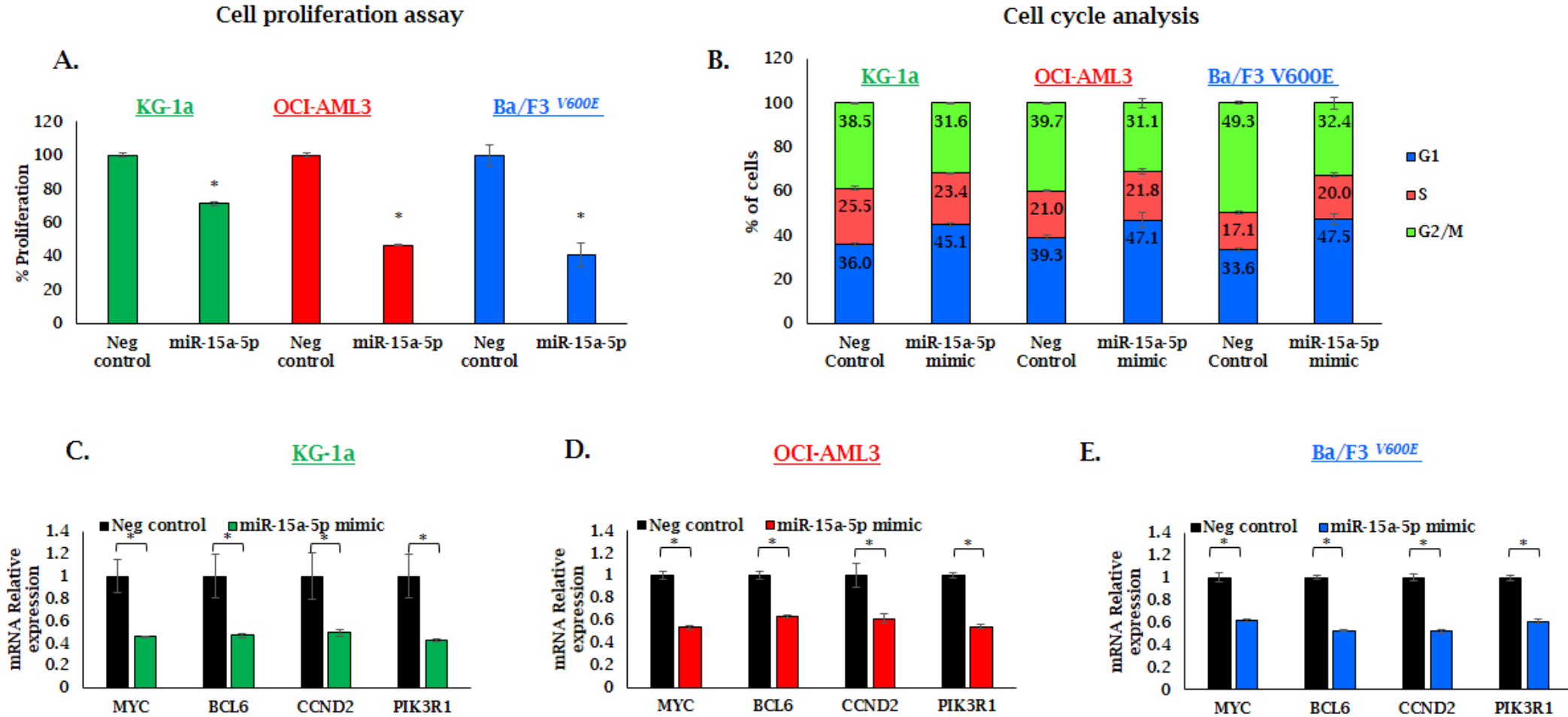
Inhibition of p-ERK signaling by miR-15a-5p and its effect on the let-7 family miRNAs



miR-15a-5p induces apoptosis in cells overexpressing MAPK-ERK pathway

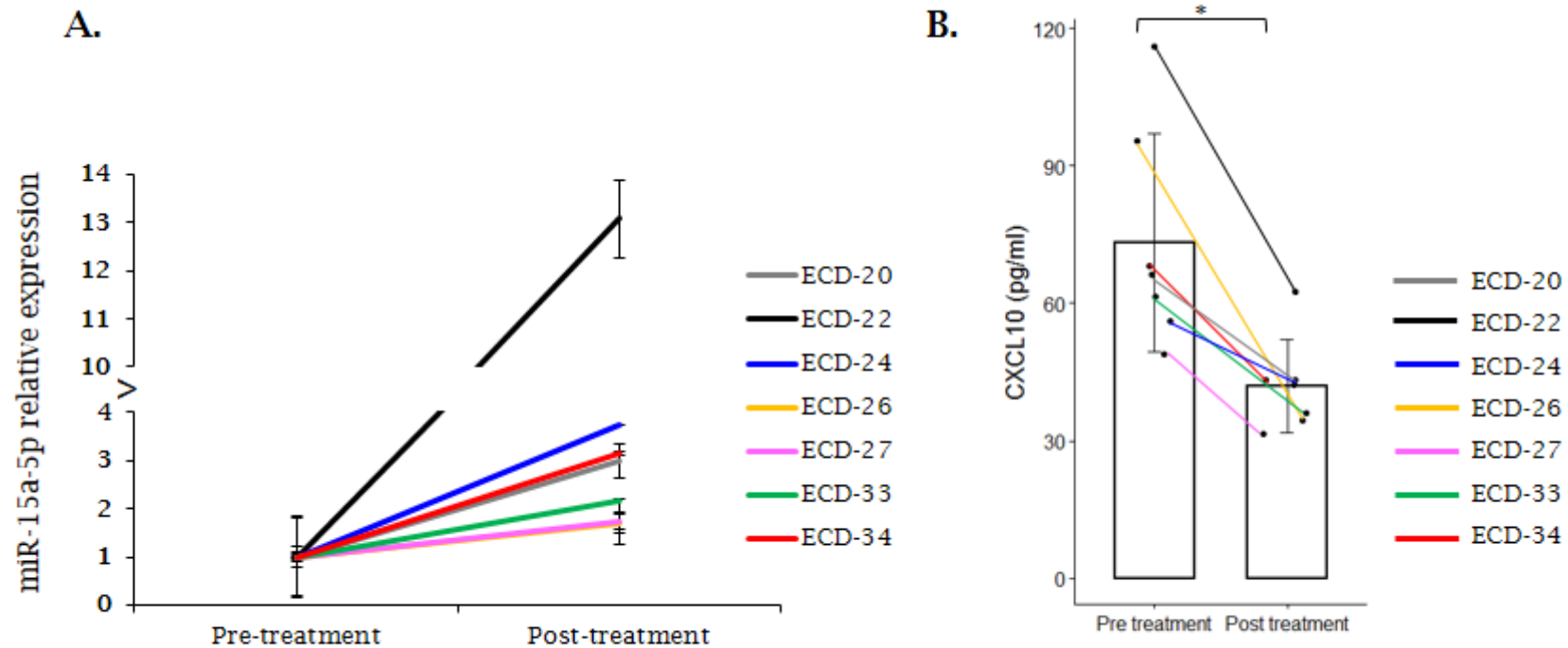


miR-15a-5p promotes growth arrest in cells overexpressing MAPK-ERK pathway



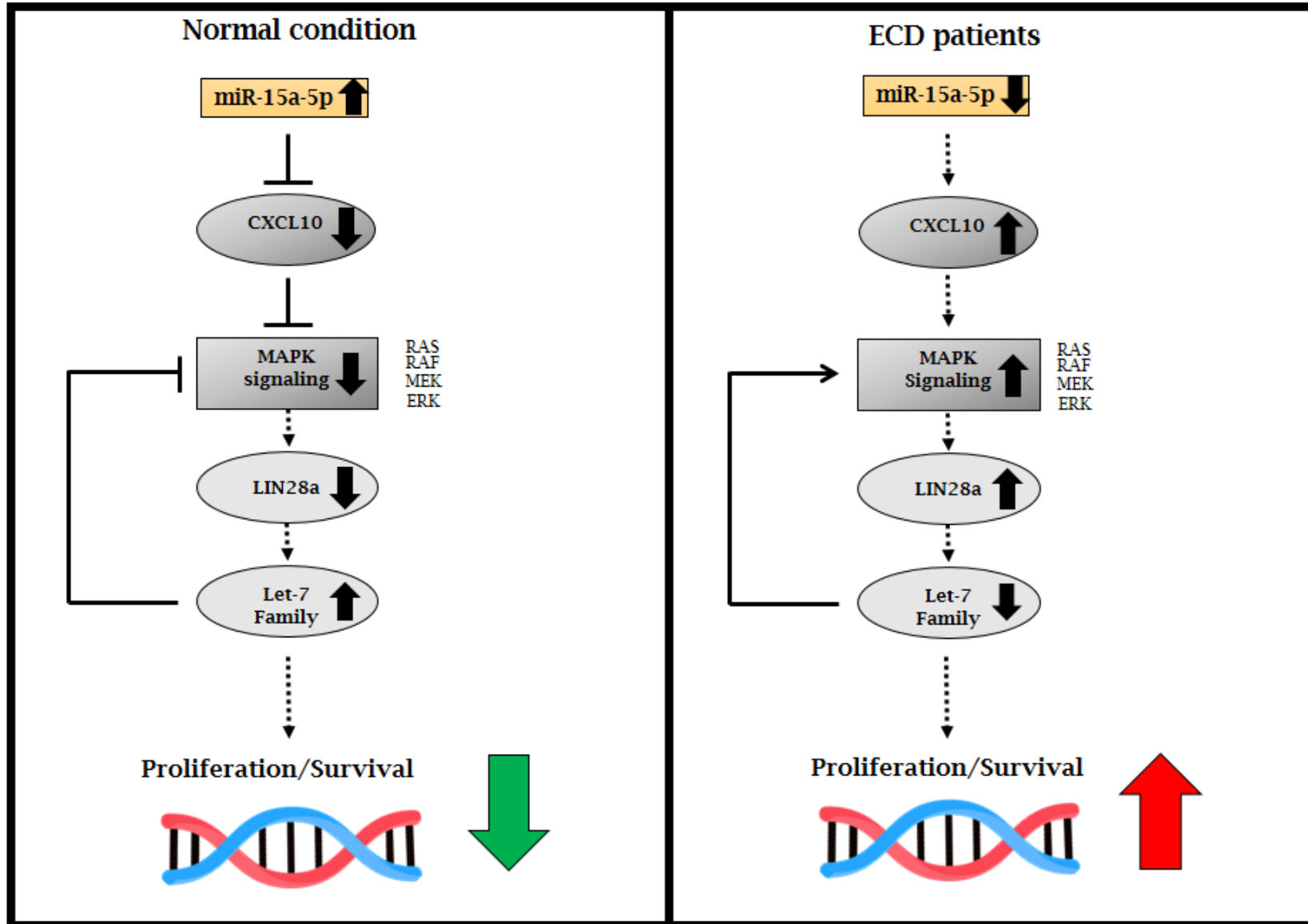
Weissman & Diamond et. al., Accepted (*Leukemia*), 2021

MiR-15a-5p and CXCL10 expression in ECD patients after treatment with MEK inhibitor



Weissman & Diamond et. al., Accepted (*Leukemia*), 2021

Suggested mechanism for miR-15a-5p involvement in ECD pathogenesis



Conclusions



- Circulating microRNAs may assist in the future for establishment of biomarkers for diagnosis and treatment response
- MicroRNAs highlights additional layers of post-transcriptional regulation in ECD pathogenesis
- miR-15a acts as a tumor suppressor by downregulating CXCL10, and down regulation of MAPK signaling through Lin-28a and the let-7 family
- Upregulation of miR-15a-5p in ECD patients may have potential therapeutic utility in the management of this disease

Our Team

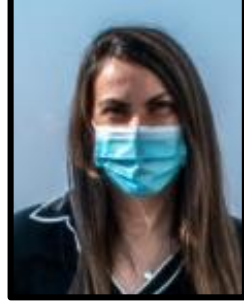
Ofer
Shpilberg



Roei
Mazor



Oshrat
Rokah



Hila
Fishov



Katarina
Mekin



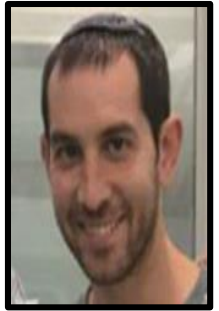
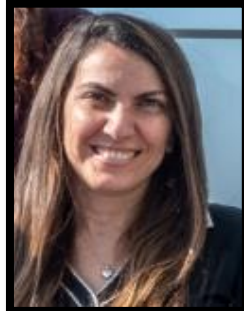
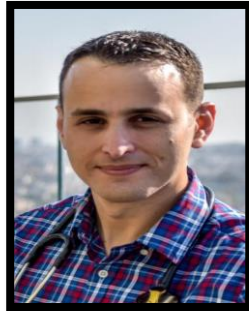
Olga
Kersy



Vered Adi
Asher-Guz



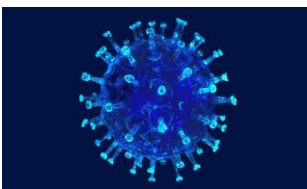
Ran
Weissman



Our Research Supports



Post-
COVID



Pre-
COVID

Big potential from small molecules this is a **miR**acle



Thank you