

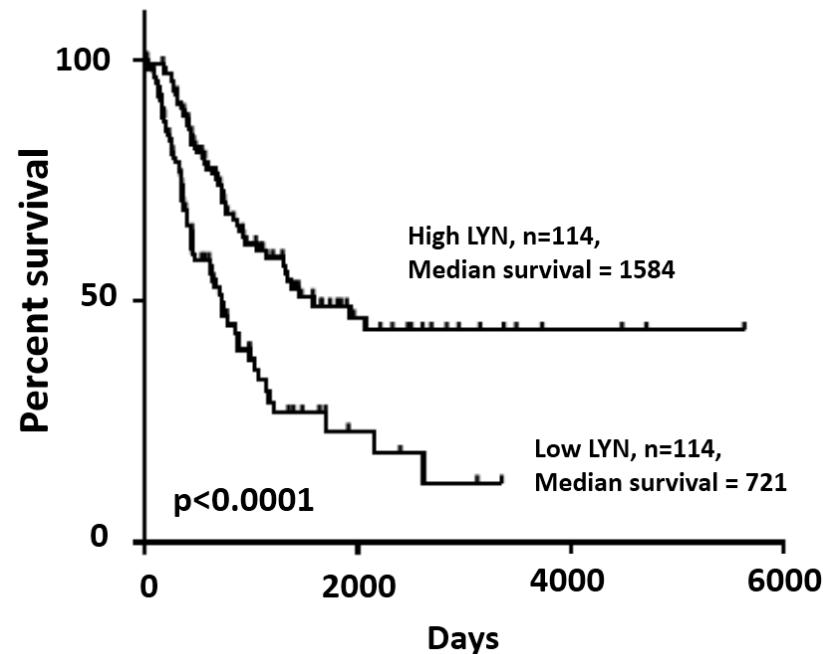


SELECTED OPPORTUNITY IN ONCOLOGY

A Lyn kinase activator for the treatment of BRAF inhibitor-resistant melanoma
(BIO18366)

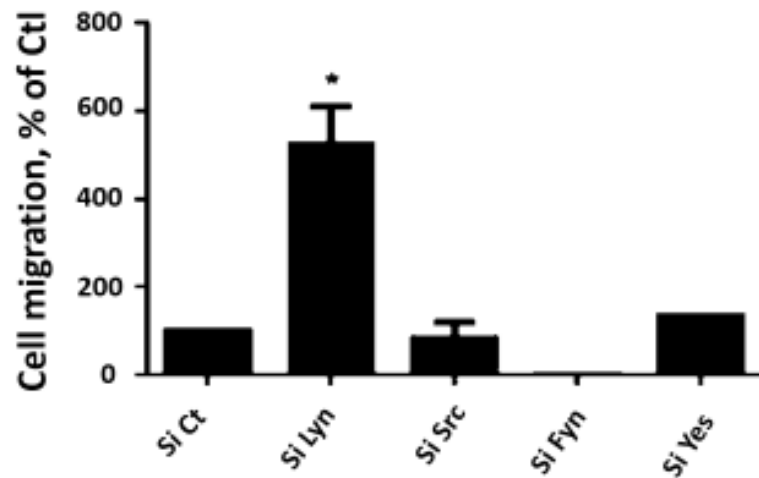
- **Target:** LYN kinase
- **Application:** Treatment of therapy-resistant melanoma
- **Potential Product** :a Lyn Kinase activator such as Tolimidone (MRL-1023) from Melior pharmaceuticals currently in phase II for diabetes
- **Rationale:**
 - Lyn expression is decreased in BRAFi-resistant melanoma cells
 - Patients with melanoma expressing high level of Lyn display a favourable prognosis
 - Lyn inhibition increases the metastatic ability of melanoma cells
 - A Lyn allosteric activator (MRL1023) inhibits the invasive properties of melanoma cells
- **Patent Applications** : PCT/EP2019/083926 :METHODS AND COMPOSITIONS FOR TREATING MELANOMA

Patients with melanoma expressing high level of LYN display a favorable prognosis



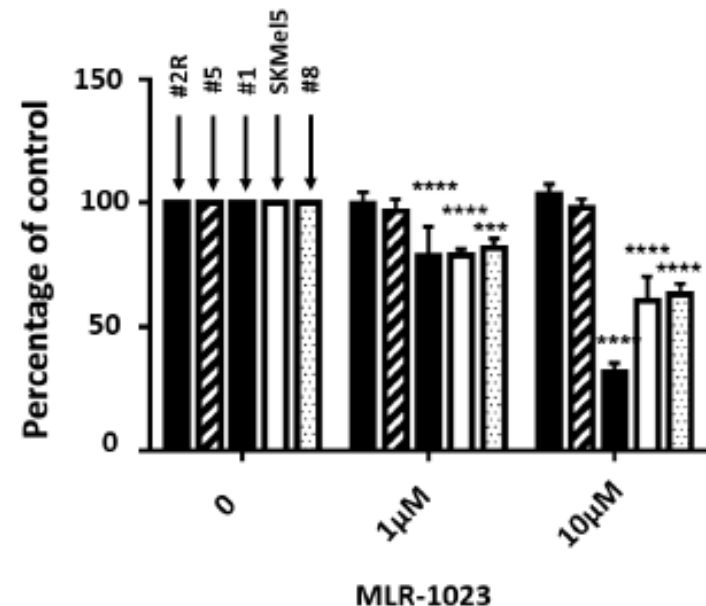
Kaplan-Meier analysis of the TCGA cohort. Patients with a low LYN expression in the tumors have a statistically significant reduced overall survival time ($p < 0.0001$, log rank test (Mantel-Cox)).

LYN inhibition increases the metastatic ability of melanoma cells

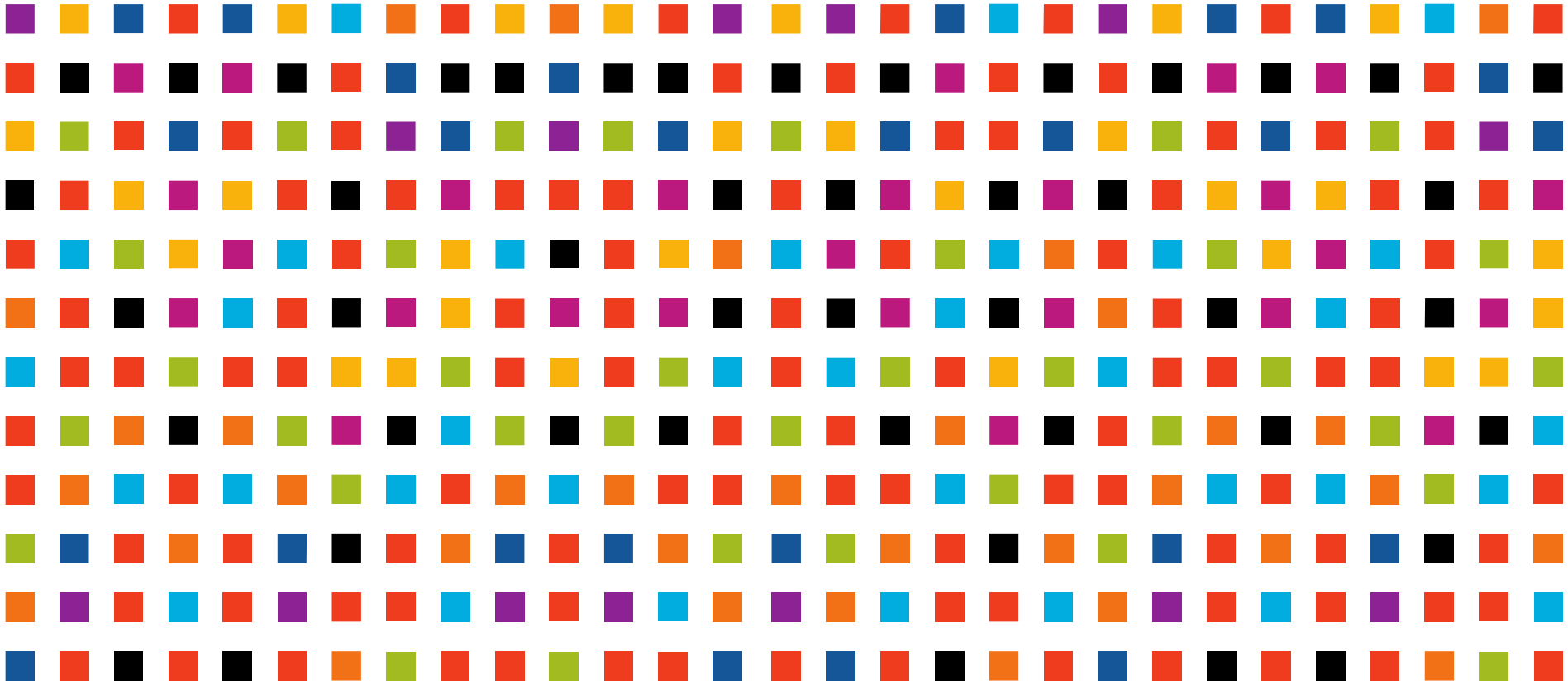


Melanoma cells expressing high level of LYN (#2) were transfected with various kinase siRNA and assessed for motile ability using Boyden chamber experiments

LYN allosteric activator, MLR1023 inhibits the invasive properties of melanoma cells



Quantification of the effect of MLR1023 on migration of different melanoma cells. Note that the cells that do not express LYN (patient#2R and patient#5) were not responsive to MLR1023



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