mir-1206 micro-RNA variant is associated with methotrexate-induced mucositis in pediatric acute lymphoblastic leukemia

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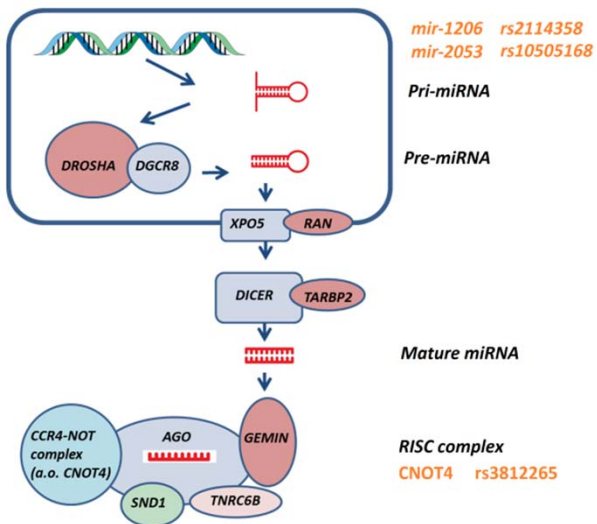
Background

- **Methotrexate (MTX)-induced oral mucositis** occurs in 20% of acute lymphoblastic leukemia patients despite folate rescue therapy.
- Three single nucleotide polymorphisms (SNPs) in **micro-RNA (miRNA)** biogenesis and processing genes were previously associated with MTX-induced oral mucositis *(Lopez-Lopez et al, 2014).*

Aim

- To **validate** the association of previously identified candidate miRNA variants in relation to MTX-induced mucositis.

Figure 1: miRNA processing pathway genes



Patients and methods

- **117** Dutch pediatric ALL patients
- Methotrexate 5 g/m^2/dose (DCOG ALL-10)
- **Prospective** collection toxicity data
- Endpoint: mucositis **grade ≥ 3**
  National Cancer Institute (NCI) criteria:
  "confluent ulcerations, bleeding with minor trauma, unable to adequately aliment or hydrate orally"
- Three candidate SNPs located in (figure 1):
  - **miRNA processing pathway genes**
  - **miRNA genes**
- Statistical analysis: χ^2 test

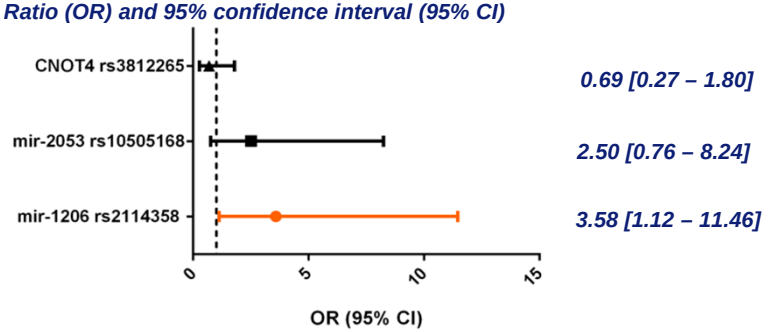
Results

- rs2114358 A>G in *mir-1206* was significantly associated with mucositis NCI grade ≥ 3 *(table 1 and figure 2)*

Table 1: genotype frequencies of statistically significant SNPs

Gene (SNP)	Genotype	No mucositis n (%)		Mucositis n (%)	
mir-1206 rs2114358	AA	31	(89%)	4	(11%)
	AG	55	(82%)	12	(18%)
	GG	9	(60%)	6	(40%)
mir-2053 rs10505168	TT	51	(84%)	10	(16%)
	TC	34	(83%)	7	(17%)
	CC	10	(67%)	5	(33%)
CNOT4 rs3812265	CC	52	(79%)	14	(21%)
	CT	40	(85%)	7	(15%)
	TT	3	(75%)	1	(25%)

Figure 2: forrest plot of studied SNPs in relation to mucositis with Odds Ratio (OR) and 95% confidence interval (95% CI)



Conclusion

We confirmed the association of rs2114358 A>G in *mir-1206* with MTX-induced mucositis in a prospective cohort of pediatric acute lymphoblastic leukemia patients.

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