



7° Conferenza Nazionale dei Servizi Trasfusionali

Vicenza, 24-26 maggio 2023

L'allele HLA*03:01 è predittivo di una forte risposta anticorpale a 6 mesi dalla vaccinazione anti-Covid-19: risultati dallo studio osservazionale prospettico "RENAISSANCE"

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Vicenza - 25 maggio 2023



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- Since the beginning of SARS-CoV-2 pandemic, several studies have been conducted on HLA and Covid-19 infection and severity
- Conversely, few investigated the role of HLA polymorphism on vaccine response
- Age and gender are predictive of anti-Spike IgG titers at day +14 after mRNA vaccination



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Polymorphism of the HLA system and weak antibody response to BNT162b2 mRNA vaccine

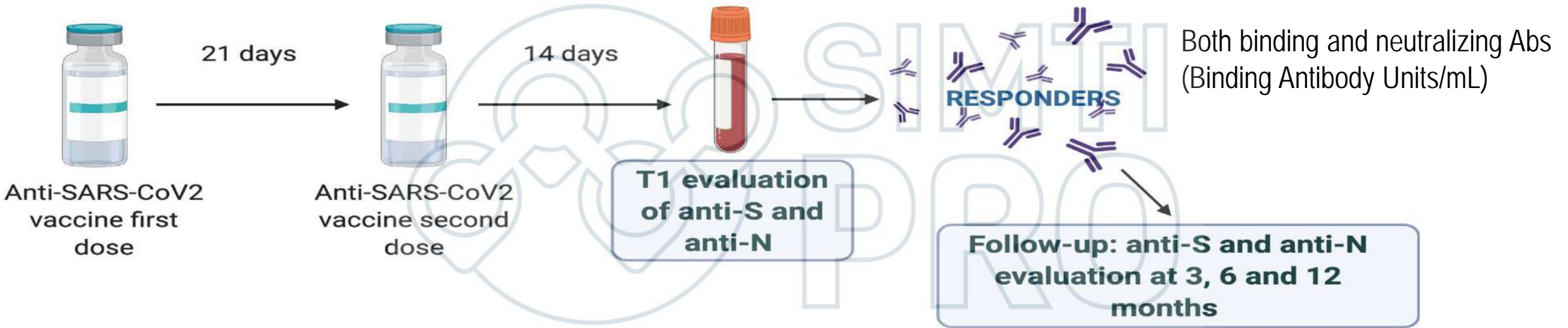
35th European Immunogenetics & Histocompatibility Conference
Amsterdam - 19th May 2022

	Study sample	Reference population	P-value	
Locus A			$\alpha/m = 0.0042$	
	03:01 g	3.6036	0.0007	
	33:03 g	2.2523	0.0021	
Locus B			$\alpha/m = 0.0026$	
	58:01 g	4.955	0.0014	
	35:02 g	4.955	0.0445	
	37:01 g	3.1532	0.0216	
Locus C				
	05:01 g	2.7027	5.773	0.0499
Locus DRB1				
	03:01 g	5.4054	9.4723	0.0385
	16:01 g	8.1081	4.9572	0.0307



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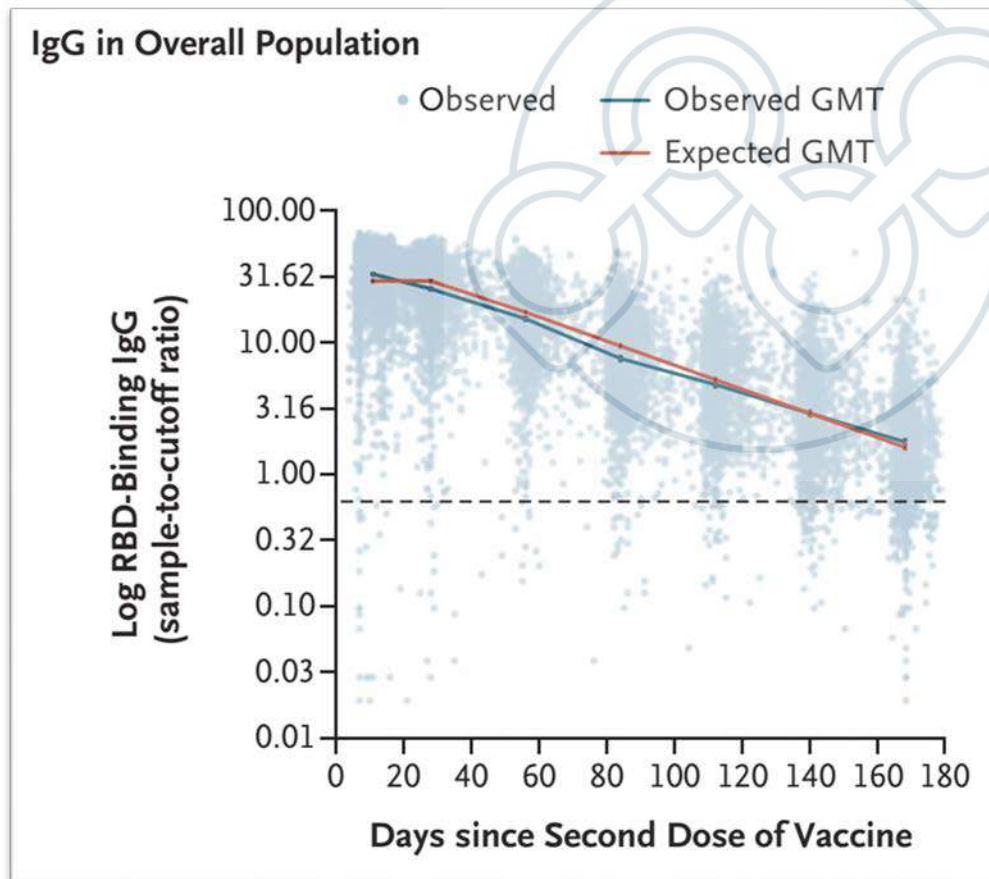
Primary endpoint: anti-S IgG antibodies at 14 days after 2nd dose



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- Follow-up: anti-S anti-N evaluation at 3, 6 and 12 months



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel

On July 30, 2021, the administration of a third (booster) dose of the BNT162b2 messenger RNA vaccine (Pfizer–BioNTech) was approved in Israel for persons who were 60 years of age or older and who had received a second dose of vaccine at least 5 months earlier. Data are needed regarding the effect of the booster dose

Levin EG et al., NEJM 2021

Bar-On YM et al., NEJM 2021



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- HLA typing of health care workers enrolled in the RENAISSANCE study having anti-S titers above the 95th percentile at six months after vaccination (out of n=2,569 enrolled in the study)
- Individuals with clinical history of Covid-19 or positive anti-N antibodies were excluded



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- HLA typing: two-field HLA-A, -B, -C, DRB1 (G groups)
- Allelic frequencies were compared with those of weak responders (anti-S titers <5th perc. at day +14) and of general population, taken from the national bone marrow donor registry, IBMDR
- Multivariate analysis: age, gender, BMI

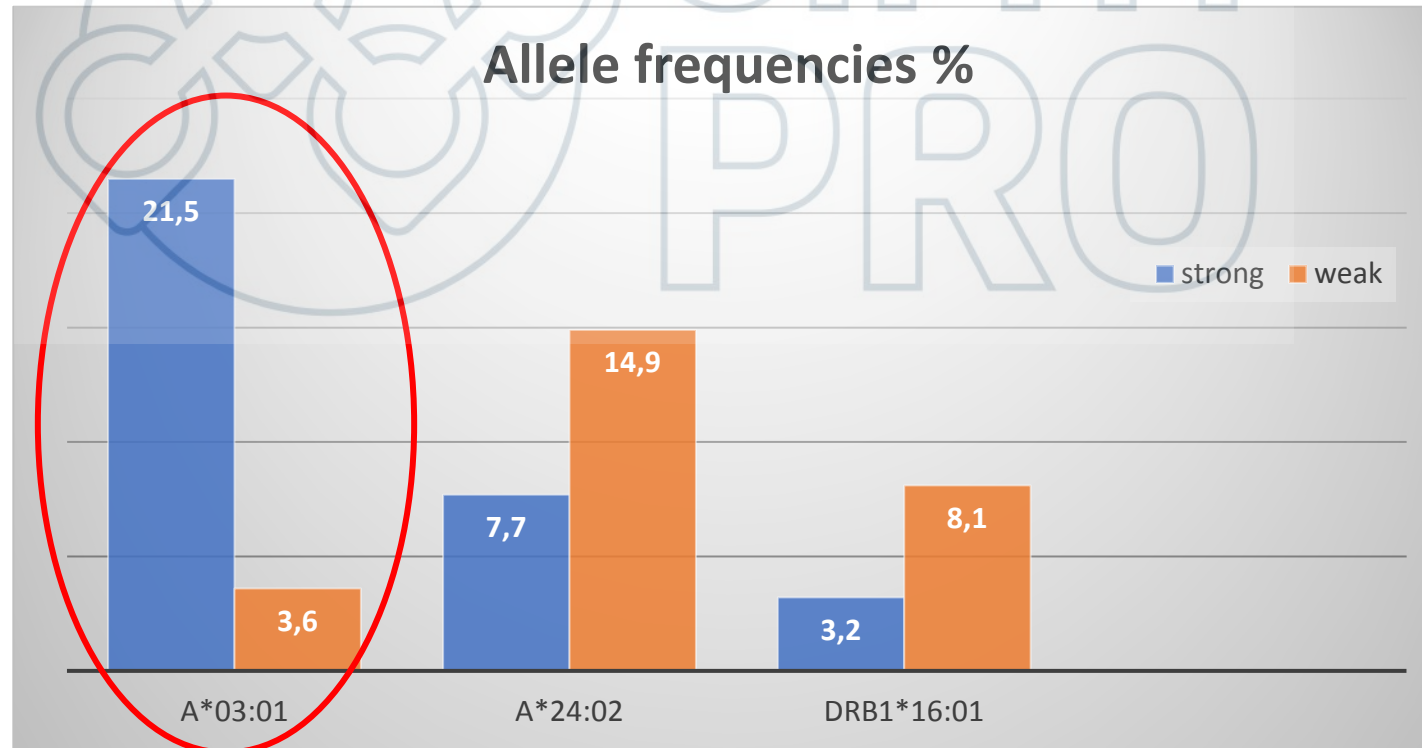


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- n=123 evaluable individuals, one-third with IgG anti-S >2,080 BAU/mL (lowest value of 1,261 BAU/mL) → «strong» responders vs. «weak» responders (n=111 already HLA typed)

IBMDR:
10.6%





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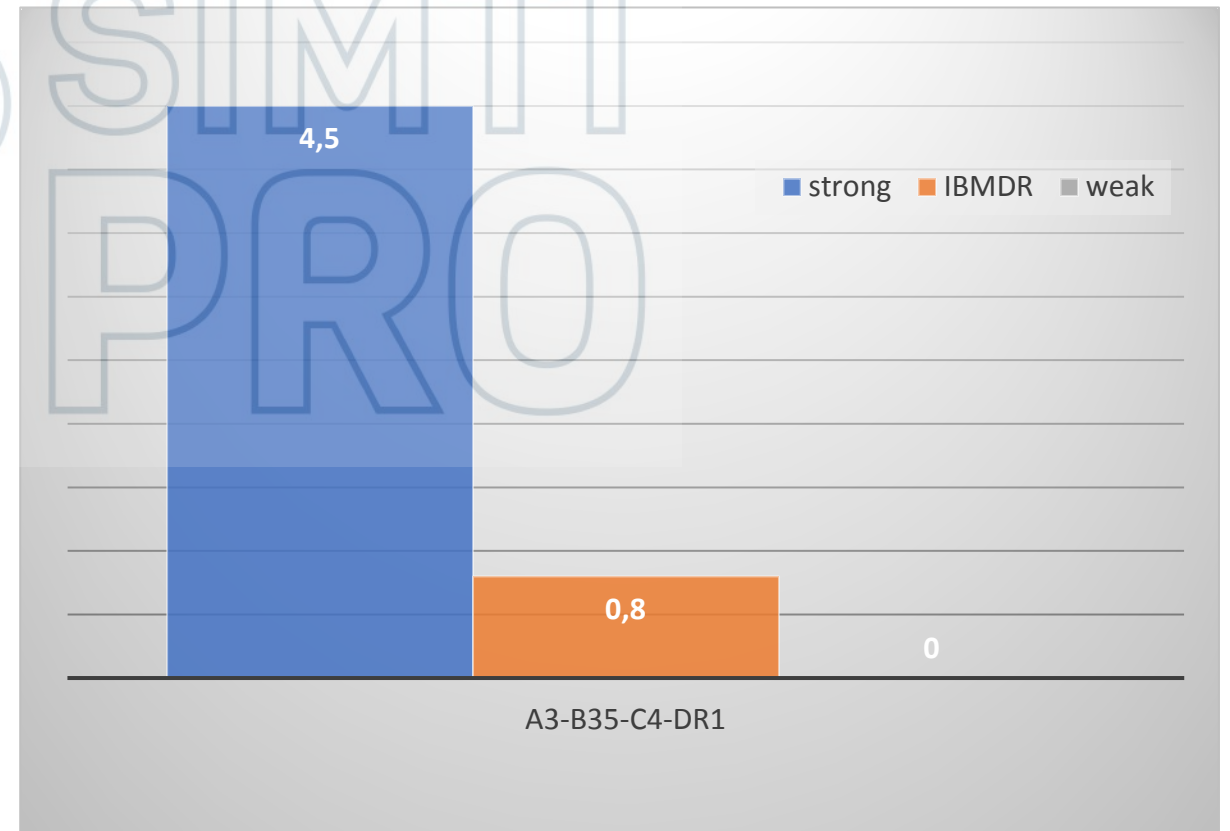
- After multivariate analysis HLA-A*03:01 confirmed to be statistically significant ($p < 0.0001$) and was predictive of high antibody titers at 6 months with an OR of 12.5 with respect to weak antibody levels
- Age was the only other significant variable



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- Ancestral haplotype A3~B35~C4~DR1
- A*03:01, :02
B*35:01, :03, :04, :08
C*04:01
DRB1*01:01, :02, :03, :11

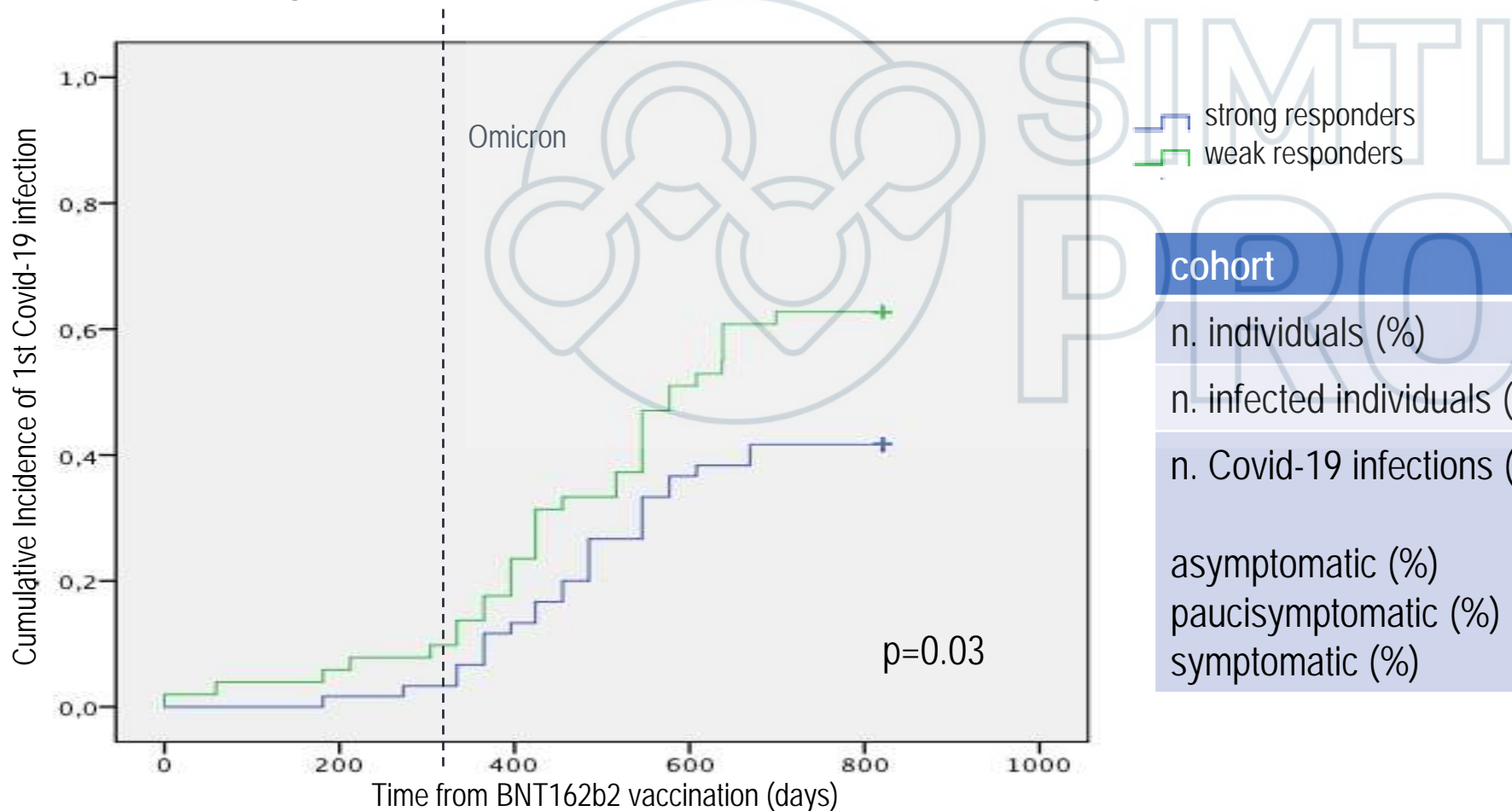




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- Looking for a correlation with protection against Covid-19 infection...



cohort	strong resp.	weak resp.
n. individuals (%)	61 (100)	52 (100)
n. infected individuals (%)	26 (42)	32 (61)
n. Covid-19 infections (%)	28 (100)	37 (100)
asymptomatic (%)	4 (15)	3 (8)
paucisymptomatic (%)	6 (21)	6 (16)
symptomatic (%)	18 (64)	28 (76)

courtesy of Dr. Lara Crucitti



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- HLA-A*03:01 confirms to be a significant independent predictor of strong humoral response after BNT162b2 vaccination among n=2,569 individuals enrolled in the prospective observational study RENAISSANCE
- The ancestral haplotype A3~B35~C4~DR1 is more represented among the individuals with a strong humoral response compared with the reference population of over 120,000 healthy hematopoietic stem cell donors. The same haplotype is absent in the group of weak responders
- HLA-A*03:01 and the ancestral haplotype might be involved in the antibody production after BNT162b2 mRNA vaccine, together with the age of vaccinees



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- The anti-Spike antibody titers at 6 months after vaccine correlate with Covid-19 infection, both in terms of number of infections and of severity of clinical presentation
- The identification of HLA-A*03:01 allows for the stratification of vaccinees according to the expected humoral response and risk of breakthrough infection and severity
- These data highlight the role of HLA polymorphism on response after vaccination, confirming its relevance for SARS-CoV-2



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SIMT



SIMT

RENAISSANCE team

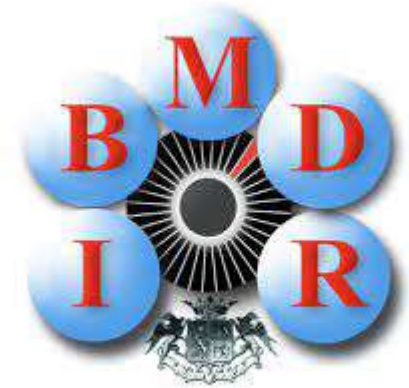
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