

RELA-Associated Autoinflammatory Disease (RAID)

– Clinical Case Studies and Therapeutic Approaches

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I BACKGROUND:

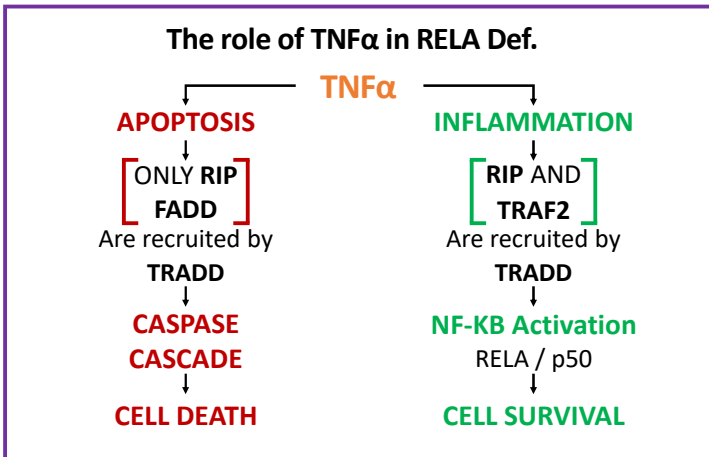


Figure 1: Simplified schematic presentation of TNF-alpha/NF-kB pathway

- *RELA* haploinsufficiency results in TNF-dependent chronic mucocutaneous ulceration and autoimmune disorders
- Enhanced TLR7-driven secretion of type I interferons (IFNs) and interferon-stimulated gene expression play key role in disease pathophysiology
- Dominant-negative variants in *RELA* present novel form of type I interferonopathy with systemic auto-inflammatory and autoimmune manifestations
- To date individuals from only eight families have been described in literature

II CASE PRESENTATION:

We compare three non-related cases of RAID treated in pediatric rheumatology departments in Germany:

#	AGE/SEX	ONSET	GENETIC VARIANT	SYMPTOMS	TREATMENT	RESPONSE
1	17 year old female	Childhood	c.1515_1516del p(Ala507Profs*25)	Ulcers, rash, headache, joint pain, fatigue	Immunosuppression: - Etanercept - Baricitinib - (Adalimumab)	Minimal response to Etanercept
2	2 year old male	4 Month	c.592C>G p(Arg198*)	Fever	None	Self-limiting course of disease
3	1.5 year old female	Infancy	c.506C>G p(Ser169*)	Severe enteropathy, lymphadenopathy, eczema	Immunosuppression: - Dupilumab Diet	Significant improvement

Table 1: Overview of patient characteristics, genetic findings and treatment approach

III CONCLUSION:

- Inborn errors of the NF-κB pathways underlie various clinical phenotypes
- *RELA*-associated autoinflammatory disease (RAID) shows great heterogeneity in clinical presentation
- Management strategies include dietary recommendations, TNFα -blockade and JAK-inhibition and must be carefully tailored to each patient's clinical manifestations
- Long-term disease course remains to be seen

Literature: Badran et al., Human *RELA* haploinsufficiency results in autosomal-dominant chronic mucocutaneous ulceration, J. Exp. Med. 2017 Vol. 214 No. 7 1937–1947; Moriya et al., Human *RELA* dominant-negative mutations underlie type I interferonopathy with autoinflammation and autoimmunity, J. Exp. Med. 2023 Vol. 220 No. 9