IMMUNOPSYCHIATRY: STUDYING INFLAMMATORY RESPONSE IN PSYCHIATRIC DISORDERS – FINDINGS FROM ÖREBRO UNIVERSITY

SANE Sweden 2019 PANS Conference

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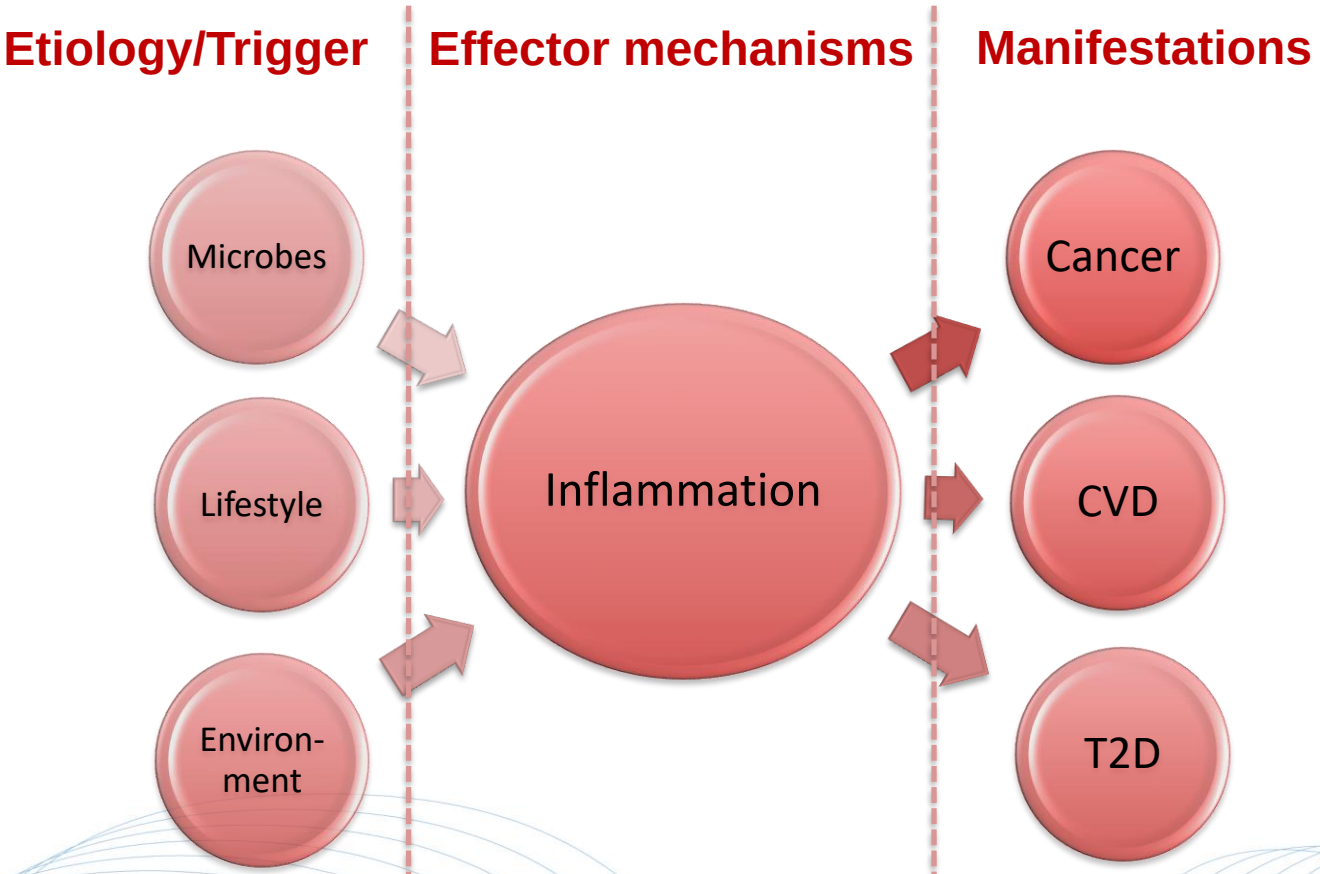
Inflammation

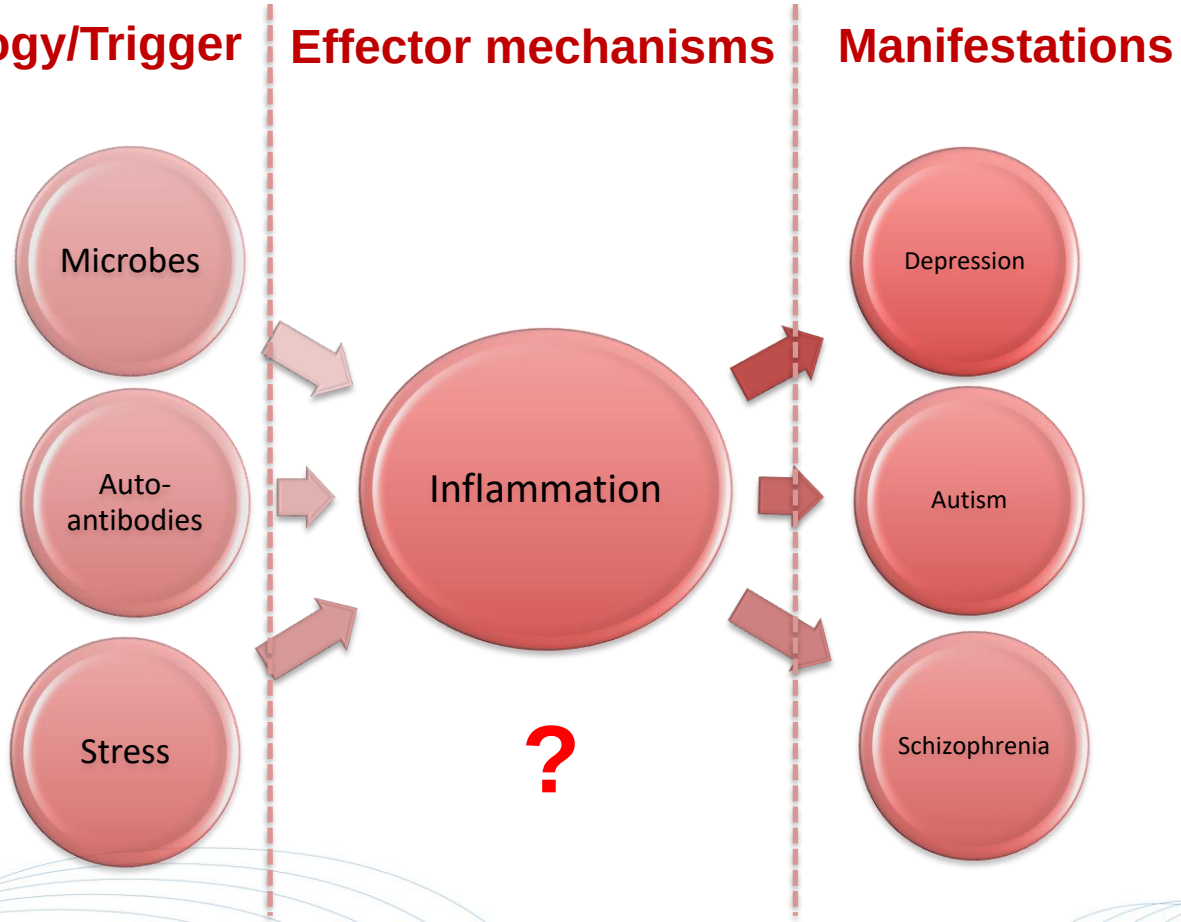
"Functionally, inflammation is broadly defined as a protective **response** of the organism to stimulation by invading pathogens or endogenous signals……. However, due to the complex and often simultaneous molecular, immunological and physiological processes involved in the inflammatory reaction, **a clear definition of inflammation presents a challenge."**

- Netea et al*, Nat Immunol, 2018*

Inflammation



Inflammation in psychatric disorders



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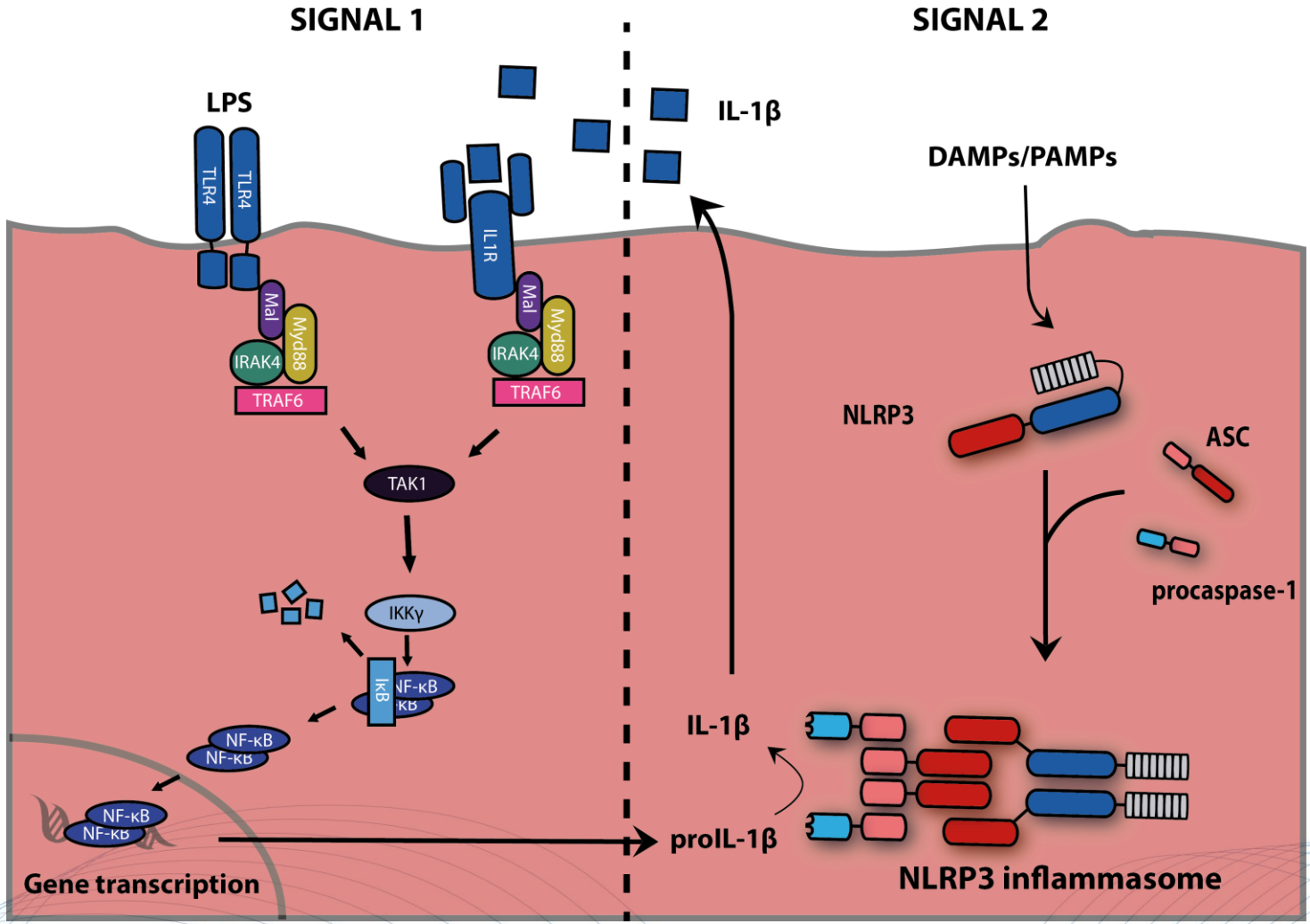
NLRP3 inflammasome

- IL-1 family cytokines (IL-1β) has been shown to be increased in several psychiatric disorders
- Inflammasomes are activated by many triggers (microbial, endogenous and exogenous) – especially the NLRP3 inflammasome
- Inflammasome is tightly regulated

NLRP3 inflammasome



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Could activation of the NLRP3 inflammasome axis act as a common denominator in markedly ill psychiatric patients?

40 psychiatric patients and 40 healthy controls

- Schizophrenia spectrum disorders (n=14)
- Autism spectrum disorders (n=8)
- Obsessive-compulsive disorder (n=10)
- Non-suicidal self-injury disorder (n=8)

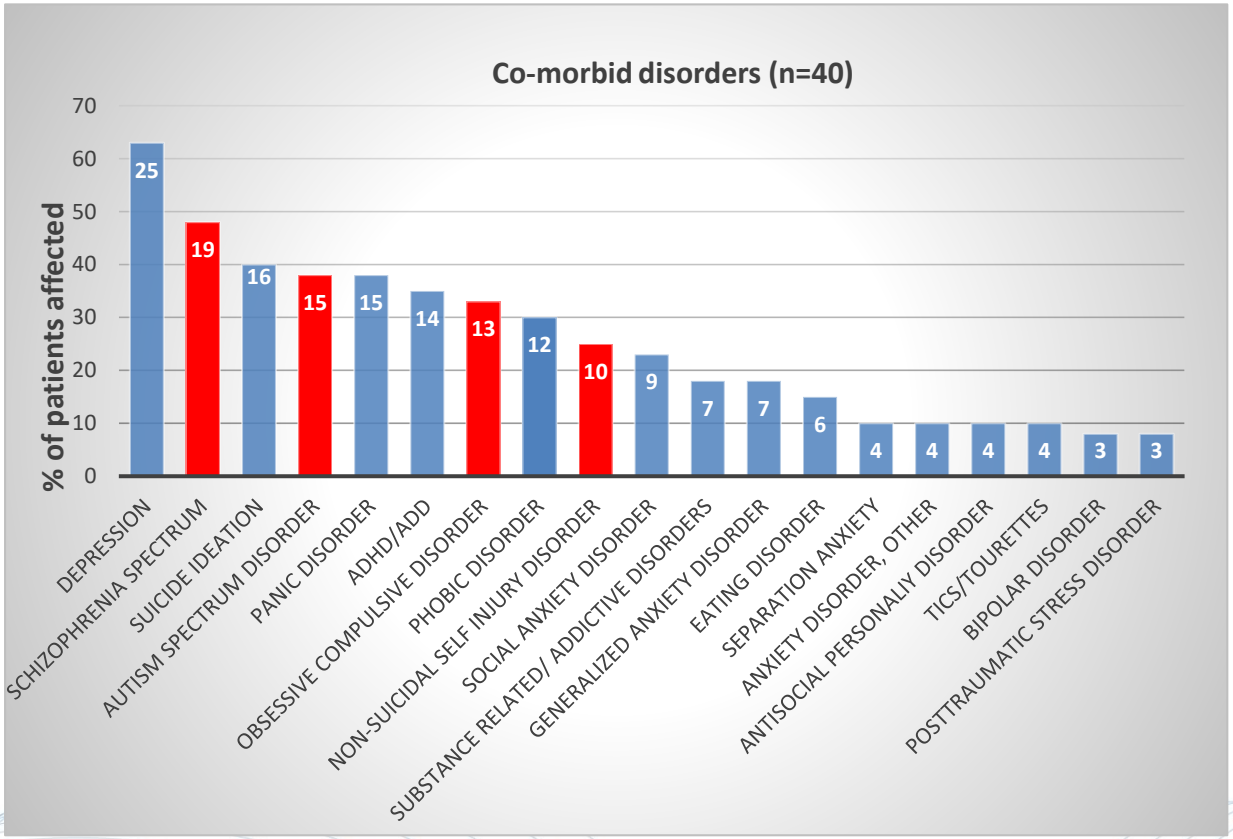
While different primary diagnoses, homogenous regarding severity and inability to function in the daily life

	SSD	ASD	OCD	NSSID
WHODAS 2.0 (median, range)	65 (41-100)	83 (27-100)	73 (58-85)	64 (33-81)
CGI-S (median, range)	5 (3-7)	5,5 (3-7)	5 (1-6)	5 (2-6)

Hylén et al., under review

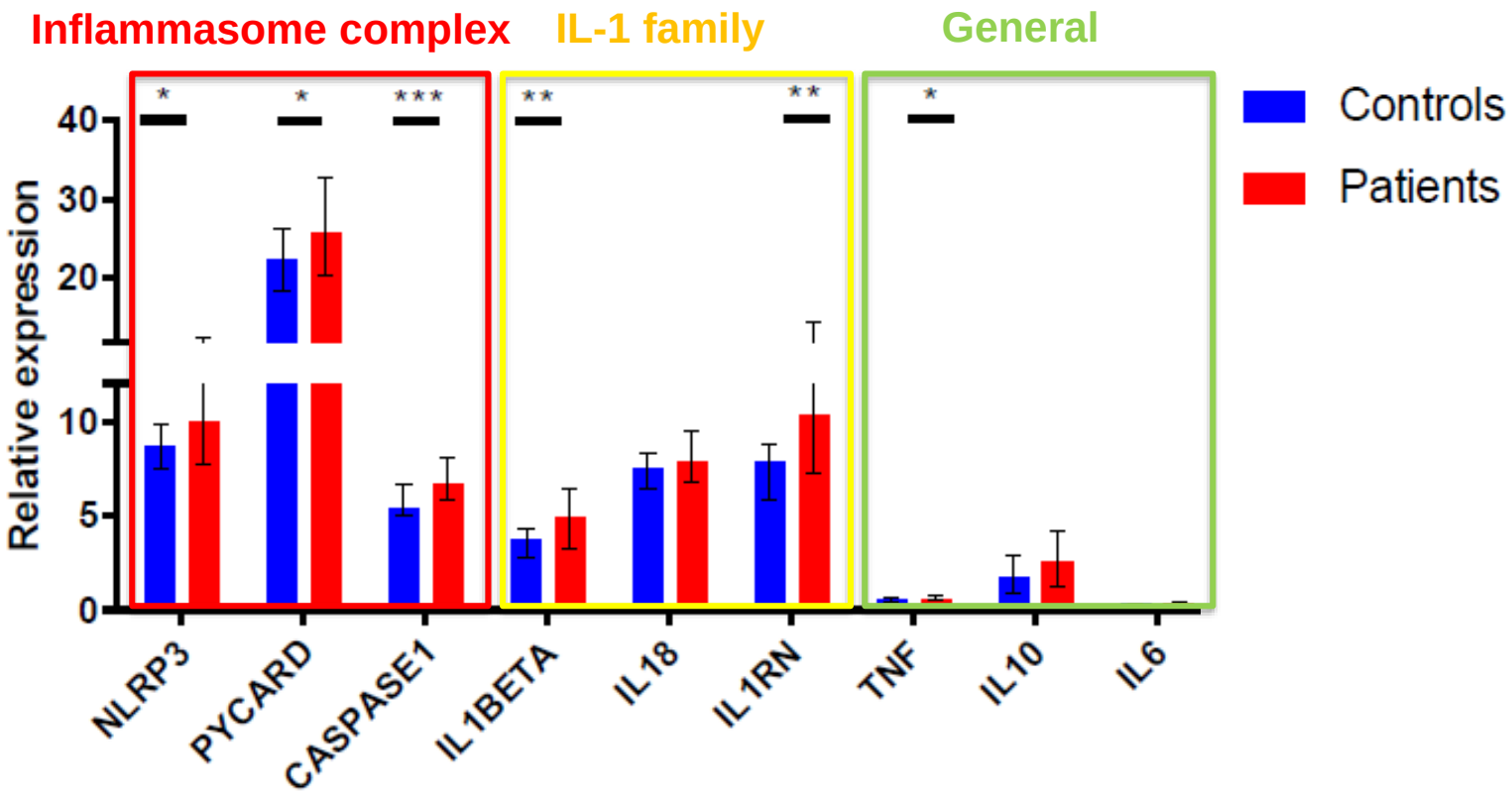
Comorbidity

Highly comorbid – half of the patients fulfilled at least 5 diagnoses



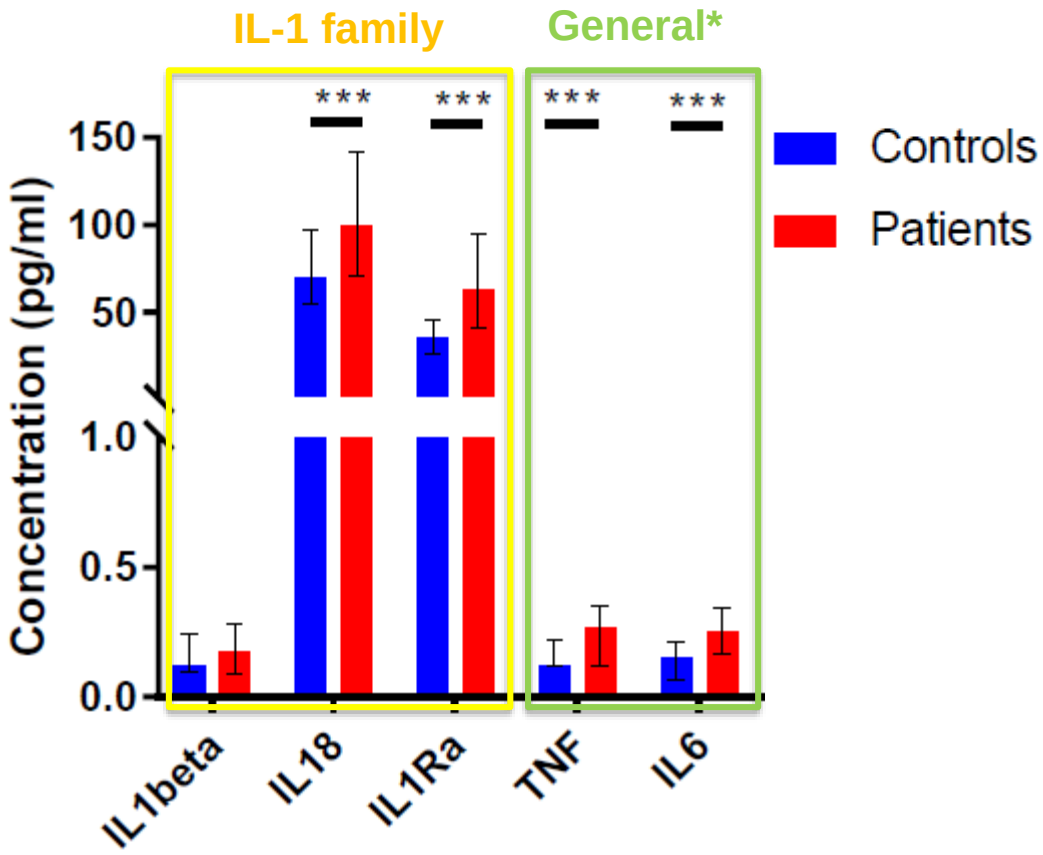
Hylén et al., under review

Priming state – signal 1



Hylén et al., under review

Cytokine production – signal 2



**** IL-10 ND***

Hylén et al., under review

Increased activity – increased severity?

Correlation between severity and inflammasome activity – in patients

		CGI-S	WHODAS 2.0
Gene expression	*PYCARD*	*0.34; p=0.035*	ns
	CASP1	ns	*0.36; p=0.037*
	IL18	*0.44; p=0.004*	ns
	IL1RN	*0.33; p=0.037*	ns
	IL1B	*0.32; p=0.046*	ns
Protein	IL-1Ra	ns	*0.35; p=0.045*

Hylén et al., under review

Conclusions

Circulating immune cells in markedly, ill psychiatric patients are primed with the respect to the inflammasome, which partially translated into increased levels of cirulating cytokines

While correlations between immune markers and disease severity was rather weak, all correlations were found to be IL-1 family cytokines and inflammasome components

The NLRP3 inflammasome, irrespective of etiology, could serve as a driver of inflammation in severe psychiatric disease with high comorbidity

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Thank you for your attention!