Blood and Brain Tissue Biomarkers for Autoimmunity and Inflammation in Suicidal Behavior and Suicidal Ideation

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Abstract: Suicidal behavior and ideation are serious psychiatric symptoms that must be taken seriously and that can trigger a genuine suicide if there is no timely intervention. Biomarkers that can predict such behavior are therefore incredibly important in this context. This article discusses inflammatory markers that may be elevated in patients presenting suicidal behavior. There is evidence that autoantibodies against thyroid tissue are associated with suicidal ideation and behavior. However, there are also autoantibodies against neuronal and glial antigens, that according to recent studies play an only minor role in suicidal behavior. We can therefore assume that overall, autoimmune processes in the thyroid gland play a role in suicidal behavior and suicidal ideation in association with brain function and inflammatory processes. The relationship between neural autoantibodies and suicidal behavior remains under investigated, but the first studies have indicated that suicidal behavior affects only a small minority of patients with neural autoantibodies, if any. Suicidal behavior rarely occurs as a clinical feature in autoimmune encephalitis with autoantibodies. Taken together, the studies show that in a minority of patients with suicidal behavior, pro-inflammatory markers are more prevalent than anti-inflammatory markers.

Keywords: Psychiatry, Suicidal behavior, Autoantibodies, Inflammation.

1. SUICIDAL BEHAVIORS AND IMMUNE-RELATED BIOMARKERS

Suicidal ideation and consecutive behavior are serious psychiatric symptoms that can lead to death by suicide. About 700000 people worldwide die by suicide each year (World Health Organization, 2019). However, the rate of people who attempt suicide is 20 times higher (Abou Chahla, 2023). These numbers make it clear that suicide poses a significant and life-threatening danger to humans and society. Various mental disorders are characterized by suicidal tendencies, *i.e*., severe depression and psychotic disorders. Suicidal tendencies are one of the diagnostic challenges that can only be overcome through open and honest communication with the patient and their relatives. There is much debate about the use of medication and behavioral therapy interventions for suicidal behavior and suicidal thoughts (Barker *et al*., 2025), but the assessment of biomarkers tends to take a back seat, and should therefore be given greater attention. There are currently no relevant biomarkers that can predict serious suicidality or help identify intermittent serious suicidality in individuals with chronic suicidality. This reveals a gap in diagnostic options and to close it, biomarkers are urgently needed. There are studies and meta-analysis in the field of immunological-related biomarkers demonstrating the possibility of a subtype of patients with high suicidality who exhibit increased inflammatory and autoimmune phenomena (Baldini *et al*., 2025; Serafini *et al*., 2025, Sun and Gong, 2025; Grendas *et al*., 2024; Neupane *et al*., 2023). Several studies report thyroid autoimmunity associated with increased suicide attempts (Feng *et al*., 2023; Wang *et al*., 2025; Luo *et al*., 2024). This article summarizes evidence for inflammatory and autoimmune processes in conjunction with suicide attempts and suicidal ideation. However, not discussed in this article are inflammatory processes related to infection known to be associated with a higher likelihood of suicide attempts, *i.e*., cytomegalovirus after immunoglobulin G (IgG) against the cytomegaly virus (CMV) has been detected (Dickerson *et al*., 2025; Zheng *et al*., 2023).

2. METHODOLOGY

As this brief review is a narrative review, there is no need for a detailed description of how the studies considered for this review were selected. In short, it is work relying on studies identified in PubMed in December 2025 applying the keywords “suicidality,” “suicidal behavior,” “suicide,” “biomarker,” “inflammation,” “autoantibodies,” and “antibodies” that were selected based on the author’s personal preferences.

3. THEORETICAL FRAMEWORK OF THE IMPACT OF IMMUNE DYSREGULATION ON MOOD STATE, IMPULSIVITY, AND SUICIDAL IDEATION

There is considerable evidence of altered inflammatory responses, affecting both the innate and adaptive immune systems in patients with depression (Beurel *et al*., 2020). Inflammation and inflammation markers can thus be understood as disease modifiers

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that can lead to the increased susceptibility to developing depressive symptoms (Beurel *et al*., 2020). Evidence over the last several years has shown (Lee *et al*., 2025) that stress levels, the immune system, and neurotransmitter changes can all affect the relationship between aggression, impulsivity, and suicide. Research has also revealed subtypes of reactive aggression and proactive aggression, each contributing to a patient's overall suicide risk. Although other factors such as impulsivity also play an important role in the suicide risk, it is apparently primarily task-related impulsivity and not self-reported suicidality that can determine the degree of suicide risk (Lee *et al*., 2025). Overall, there is a very complex interaction between aggression, impulsivity, and suicidality that is believed to be modulated by an immune system dysregulated by proinflammatory cytokines. Suicidal behavior is thus primarily controlled by behavioral traits such as aggression and impulsivity that in turn are associated with early childhood trauma or genetic factors. There is a distinction between factors that affect suicidal behavior only indirectly, as a model by Brundin demonstrated (Brundin *et al*. 2017). These include factors that influence the immune response, such as autoimmune diseases, infections, traumatic brain injury, vitamin D deficiency, and stress. These factors, in turn, modulate inflammatory cytokines. The cytokines can alter downstream effectors such as the kynurenine pathway, monoamine metabolism, and the hypothalamic–pituitary axis (HPA) (Brundin *et al*., 2017). The kynurenine pathway can in turn influence microglia activity and trigger glutamate hyperactivity, which can then modulate suicidal behavior (Brundin *et al*., 2017). It is also assumed that other downstream effectors such as monoamine metabolism and the HPA axis also influence suicidal behavior (Brundin *et al*., 2017). This is how immune dysregulation can lead to suicidal behavior.

4. INFLAMMATORY MARKERS, IMMUNE CELLS AND SUICIDALITY

The detection of biomarkers of inflammation and examination of immune cells in patients with suicidal ideation and behavior can only provide limited insight into underlying immunological processes even when demonstrated in large cohorts, as these are associations that in most cases suggest no causality between suicidal thoughts and behavior and the inflammation severity. Nevertheless, such associations may be important for conducting studies that, for example, use animal models to test causal relationships, or evaluate the predictive value of biomarkers employing various regression models and machine learning. There are small and large cohort studies on this topic, but surprisingly, a data-driven cluster analysis of a small cohort of patients with peripheral mononuclear cell determination revealed the increased presence of a specific sub-cell cluster, namely gamma-delta T cells, in suicidal adolescents (Fatt *et al*., 2022). Such gamma-delta T cells play an important role in maintaining health and in the development of disease (Bychkow and Wiest, 2025). Such high-dimensional phenotyping could therefore be crucial for future studies on suicidal behavior. Another working group found that proinflammatory interleukins such as interleukin-4 (IL-4) were lower in patients with severe depressive episodes and suicide attempts than in healthy controls, and that IL-4 correlated with the severity of depression in this cohort of young adults and adolescents (Jha *et al*., 2020). Various proinflammatory cytokines have been identified that are elevated in patients with suicidal behavior, which could indicate at least a mild inflammatory process in such patients. Several reviews (Baldini *et al*., 2025; Serafini *et al*., 2025) show that elevated levels of inflammatory markers are associated with an increased risk of suicide. Interleukin-6 (L-6) and tumor necrosis factor alpha (TNF-α) are biomarkers with elevated levels in serum (Castillo-Avila *et al*., 2022; Jiang *et al*., 2022); there is also a panel of biomarkers including C-reactive protein (CRP) and C-X-C motif chemokine ligand 2 **(**CXCL-2) in addition to IL-6 and TNF-alpha which can predict the suicide risk (Yang *et al*. 2024). However, other biomarkers are associated with decreased levels in patients with an increased risk of suicide, such as interleukin-2 (IL-2), interleukin-8 (IL-8) (Baldini *et al*., 2025; Serafini *et al*., 2020) or IL-4 (Serafini *et al*., 2020), in contrast to elevated levels as indicating a higher suicide risk, such as IL-6 (Baldini *et al*., 2025; Serafini *et al*., 2025). Interferon-gamma is another biomarker reportedly associated with an increased risk of suicide, but it is currently unclear whether this is associated with elevated (Baldini *et al*., 2025) or reduced levels (Serafini *et al*., 2025). A meta-analysis of 36 studies involving 2679 patients showed that patients revealing suicidal behavior presented higher CRP blood levels than healthy controls, but also than patients with depression or any other psychiatric disorder (Neupane *et al*., 2023). IL-6 was also higher in patients with suicidal behavior than in healthy controls and psychiatric patients without suicidal behavior (Neupane *et al*., 2023). In addition to these often replicated findings, another study showed a significant increase in monocytes and the ratio of monocytes to lymphocytes (Grendas *et al*., 2024), and higher levels of triggering receptor expressed on myeloid cells 2 (TREM2) in the plasma of patients with suicidal thoughts and suicide attempts compared to controls (Grendas *et al*., 2024). All these studies show that various proinflammatory cytokines and other immune markers can be predictive on an individual basis in patients with suicidal behavior and down- and upregulations of plasma levels, but this

has not been verified in large cohorts. Initial data is available from the large-scale study (Sun and Gong, 2025) involving 30911 participants in which they conducted subgroup analyses between suicidal ideation and the presence of a new inflammatory marker, RAR. This RAR marker refers to the red blood cell distribution width to albumin ratio. This working group demonstrated a positive linear relationship between RAR and suicidal ideation (Sun and Gong, 2025). This evidence supports the assumption of mild inflammation associated with suicidal thoughts. However, whether this is a cohort phenomenon that could be replicated in a European cohort remains to be seen. Inflammation may be limited to certain markers, as a significantly smaller cohort of 221 patients showed that common inflammation markers such as CRP, albumin, neutrophils, lymphocytes, monocytes, platelets, and red cell distribution width, neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio, platelet-to-lymphocyte ratio, CRP-to-albumin ratio, and neutrophil-to-albumin ratio did not differ between patients with suicidal thoughts and a history of suicide attempts, and a group without suicidality (Elbay *et al*., 2025). These results reveal very inconsistent findings indeed, as well as evidence arguing against inflammatory processes in suicidal behavior. However, note that several inflammatory markers such as IL-4, IL-6, TNFalpha, CRP, and CXCL-2 have been proven to be elevated while others such as IL-2 or IL-8 may be reduced in suicidal behavior. It therefore remains unclear at present which proinflammatory processes trigger suicidal behavior, and whether anti-inflammatory processes also promote such behavior. Ultimately, however, there is strong evidence from the majority of investigations that proinflammatory processes predominate over anti-inflammatory processes via increased levels of proinflammatory interleukins such as IL-4, IL-6, TNF-alpha, CRP, and CXCL-2, and that anti-inflammatory processes play a subsidiary role. However, cytokines have not exhibited any no specific pattern of cytokines associated with suicidal bevaior. Larger cohorts are needed to identify such patterns. In addition to changes in cytokines (predominantly increased), there are blood cell anomalies (higher proportions of monocytes and an increased monocyte/lymphocyte ratio) in patients presenting more pronounced suicidal behavior and ideation both as a cross-sectional and lifetime condition, as a multicenter study of 105 patients revealed (Grendas *et al*., 2024). That these biomarker changes can be affected by potential moderators such as diagnosis, age, gender, and medication status is very likely. This must be considered in each case and can therefore have a significant impact on the increase or decrease in biomarkers in suicidal behavior.

5. THYROID AUTOIMMUNITY AND SUICIDALITY

Considering thyroid autoimmunity: several recent studies have suggested a strong association between suicidal behavior and thyroid autoimmunity, as briefly described below. Several studies suggest a strong association between various thyroid autoantibodies and the presence of suicidal behavior that is delineated in this section. Thyroid autoantibodies are therefore identified more frequently than any other form of autoantibodies in connection with suicidal behavior and suicidal thoughts. A large study involving 1718 patients who had suffered their first episode of major depressive disorder and had not been treated for depression was divided into those who had attempted suicide and those who had not. Patients who attempted suicide had a higher symptom burden, including psychotic symptoms, and higher levels of thyroid-stimulating hormone (TSH), thyroglobulin (TG), and thyreoperoxidase (TPO) autoantibodies (Feng *et al*., 2023). Long-term data also showed that the prevalence of suicide attempts among 1701 Chinese adults was 20.2%; a multiple logistic regression analysis revealed that, in addition to clinical symptoms and the severity of clinical symptoms, the antibody level of TPO antibodies was also associated with suicide attempts. TG antibodies in particular were higher in patients who had attempted suicide (n=344) than in those who had not (n=1357). In addition, the median of TPO antibodies was also higher in patients who had attempted suicide compared to those who had not (Wang *et al*., 2025). Another study found that patients with autoimmune thyroiditis, major depressive disorder, and abnormal TSH levels were more likely to report a suicide attempt. Moreover, TPO antibodies, TSH, and anxiety were independently associated with suicide attempts in this population (Luo *et al*., 2024). This association was confirmed in another study that found that 31% of 1718 major depressive disorder patients who had attempted suicide presented elevated levels of autoantibodies against both TG and TPO compared to those with major depressive disorder who had not attempted suicide (Ren *et al*., 2025). In summary, TG, TSH, and TPO antibodies can all be associated with suicidal behavior. Moreover, thyroid function has a relevant influence on brain functions related to emotional and cognitive control, as in the right inferior orbitofrontal gyrus and right anterior cingulate cortex (Zhao *et al*., 2025), thus dysregulated thyroid hormones or thyroid antibodies could have an indirect influence on brain function relevant to suicidal behavior. Similarly, it is conceivable that thyroid autoimmunity may trigger metabolic dysregulation, which in turn could influence suicidal behavior, as metabolic dysregulation correlates with suicidal behavior (Geng *et al*., 2025). There is also evidence that thyroid function associated with low T4 levels

Table 1: Markers of Inflammation, Thyroid Autoimmunity and Neural Autoantibodies in Suicide Behavior

Biomarker	Cohort size	Effect of biomarker	Biomarker medium	Reference
Inflammatory marker				
IL-1β	N =79 suicide attempt vs. N = 123 without suicide attempt	Lower levels in patients with history of suicide attempt	Brain tissue	Serafini *et al*., 2020
IL-1β	N= 1525 patients and N =1400 controls	Lower levels in suicidal behavior and specific brain regions	Brain tissue	Serafini *et al*., 2020
IL-2	N = 130 MDD and N= 130 healthy controls	Lower levels have MDD patients with elevated suicide risk vs. healthy controls	Blood serum	Yang *et al*., 2024
IL-2	N= 1525 patients and N =1400 controls	Lower levels in suicidal behavior and specific brain regions	Brain tissue	Serafini *et al*., 2020
IL-4	N = 37 depressive patients with suicide attempts vs. N = 39 healthy controls	Lower levels in depressive subjects with suicide attempts vs. healthy controls	Blood plasma	Jha *et al*., 2020
IL-4	N= 1525 patients and N =1400 controls	Lower levels in suicidal behavior and specific brain regions	Brain tissue	Serafini *et al*., 2020
IL-6	N = 18 suicide attempt vs. N = 66 controls (no psychiatric illness and no suicide attempt)	Higher levels in suicide attempts vs. controls	Blood serum	Castillo-Avila *et al*. 2022
IL-6	N =14 with bipolar disorder and suicide attempts versus N=26 healthy controls	Higher levels in bipolar patients with suicide attempts	Blood plasma	Jiang *et al*., 2022
IL-6	N = 130 MDD and N= 130 healthy controls	Higher levels have MDD patients with elevated suicide risk vs. healthy controls	Blood serum	Yang *et al*., 2024
IL-6	N = 31 studies with participants per study ranging from 6 to 600	Elevated levels were associated with increased rik for suicide	Blood plasma or serum	Baldini *et al*., 2025
IL-6	N= 1525 patients and N =1400 controls	Higher levels in suicidal behavior and specific brain regions	Brain tissue	Serafini *et al*., 2020
IL-8	N = 130 MDD and N= 130 healthy controls	Lower levels have MDD patients with elevated suicide risk vs. healthy controls	Blood serum	Yang *et al*., 2024
TNFalpha	N = 130 MDD and N= 130 healthy controls	Higher levels have MDD patients with elevated suicide risk vs. healthy controls	Blood serum	Yang *et al*., 2024
TNFalpha	N= 1525 patients and N =1400 controls	Higher levels in suicidal behavior and specific brain regions	Brain tissue	Serafini *et al*., 2020
TNFalpha	N = 31 studies with participants per study ranging from 6 to 600	Elevated levels were associated with increased rik for suicide	Blood plasma or serum	Baldini *et al*., 2025
TGF-1β	N= 1525 patients and N =1400 controls	Higher levels in suicidal behavior and specific brain regions	Brain tissue	Serafini *et al*., 2020
CXCL-2	N = 130 MDD and N= 130 healthy controls	Higher levels have MDD patients with elevated suicide risk vs. healthy controls	Blood serum	Yang *et al*., 2024
Interferon gamma	N = 130 MDD and N= 130 healthy controls	Higher levels have MDD patients with elevated suicide risk vs. healthy controls	Blood serum	Yang *et al*., 2024
	N= 1525 patients and N =1400 controls	Lower levels in suicidal behavior and specific brain regions	Brain tissue	Serafini *et al*., 2020
RAR	N = 30911 patients	Positive linear relationship between RAR und suicidal ideation	Blood plasma	Sun and Gong, 2025
CRP	N = 130 MDD and N= 130 healthy controls	Higher levels have MDD patients with elevated suicide risk vs. healthy controls	Blood serum	Yang *et al*., 2024
CRP	N = 31 studies with participants per study ranging from 6 to 600	Elevated levels were associated with increased rik for suicide	Blood plasma or serum	Baldini *et al*., 2025

CRP	N = 2679 patients	Elevated levels in patients with suicidal behavior vs. healthy controls but also patients with psychiatric disease	Blood	Neupane *et al*., 2023
TREM2	N = 105, N =21 suicidal behavior, N = 42 history of suicidal behavior, N =42 healthy controls	Higher levels in patients with suicidal attempts and thoughts vs. controls	Blood plasma	Grendas *et al*., 2024
Gamma-delta T-cells	N =14	Gamma-delta T cells) had higher abundance in suicidal adolescents compared to healthy control	Blood plasma	Fatt *et al*., 2022
Thyroid autoimmunity marker				
TSH abs	N = 1718 patients with MDD and suicide attempt and without suicide attempt	Patients with suicide attempt and MDD had higher levels vs. MDD without suicide attempt	Blood	Feng *et al*., 2023
TG abs	N = 1718 patients with MDD and suicide attempt and without suicide attempt	Patients with suicide attempt and MDD had higher levels vs. MDD without suicide attempt	Blood	Feng *et al*., 2023
TG abs	Patients with suicide attempts (n=344) vs. those without suicide attempts (n=1357)	Higher levels in suicide attempts vs. those without suicide attempts	Blood serum	Wang *et al*., 2025
TG abs	N = 1718 with MDD and suicide attempt	Elevated levels in these patients with MDD and suicide attempts vs. MDD without suicide attempt	Blood	Ren *et al*., 2025
TPO abs	N = 1718 patients with MDD and suicide attempt and without suicide attempt	Patients with suicide attempt and MDD had higher levels vs. MDD without suicide attempt	Blood	Feng *et al*., 2023
TPO abs	Patients with suicide attempts (n=344) vs. those without suicide attempts (n=1357)	Higher median levels in suicide attempts vs. those without suicide attempts	Blood serum	Wang *et al*., 2025
TPO abs	N = 1718 patients	TPOabs were independently associated with suicide attempts	Serum	Luo *et al*., 2024
TPO abs	N = 1718 with MDD and suicide attempt	Elevated levels in these patients with MDD and suicide attempts vs. MDD without suicide attempt	Blood	Ren *et al*., 2025
Neural autoantibodies				
NMDAR abs	N=29 suicide attempters	Not found in patients with suicide attempt	CSF	Fernström *et al*., 2017
AMPAR abs	N=29 suicide attempters	Not found in patients with suicide attempt	CSF	Fernström *et al*., 2017
GABAB abs	N=29 suicide attempters	Not found in patients with suicide attempt	CSF	Fernström *et al*., 2017
LGI1 abs	N=29 suicide attempters	Not found in patients with suicide attempt	CSF	Fernström *et al*., 2017
CASPR2 abs	N=29 suicide attempters	Not found in patients with suicide attempt	CSF	Fernström *et al*., 2017
DPPX abs	N=29 suicide attempters	Not found in patients with suicide attempt	CSF	Fernström *et al*., 2017
VGKC abs	N =1 suicide attempt of 213 psychiatric inpatients vs. 173 controls	Increased suicidal ideation in patients	Serum and CSF	Kruse *et al*., 2015
Striational muscle abs	N =2 suicide attempt of 213 psychiatric inpatients vs. 173 controls	Increased suicidal ideation in patients	Serum and CSF	Kruse *et al*, 2015

Abbreviations: AMPAR abs = A-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor antibodies, CASPR2 abs = Contactin-associated protein 2 antibodies, CRP = C-reactive protein, CXCL-2 = Chemokine (C-X-C motif) ligand 2, DPPX abs = Dipeptidyl-Peptidase-like Protein-6 antibodies, GABAB abs = gamma-aminobutyric acid B antibodies, IL-1β = interleukin 1beta, IL-2 = interleukin 2, IL-4 = interleukin 4, IL-6 = interleukin 6, IL-8 = interleukin 8, LGI1 abs = Leucin rich glioma inactivated protein 1 antibodies, MDD = major depressive disorder, NMDAR abs = N-methyl-D-aspartate receptor antibodies, RAR = red blood cell distribution width to albumin ratio, TG abs = Thyreoglobulin antibodies, TGF-1β = tumor growth factor 1-beta, TNFalpha = tumor necrosis factor alpha, TPO abs = Thyroid peroxidase antibodies, TREM2 = Triggering receptor expressed on myeloid cells 2, TSH abs =Thyroidea stimulating hormone antibodies, VGKC abs = Voltage gated potassium channel antibodies.

correlates with a low to moderate risk of suicidal behavior (Saeed *et al*., 2026). This may lead to thyroid-related biomarkers revealing thyroid hormone anomalies being a risk factor for broader affective and

metabolic dysregulation potentially relevant to suicidality.

6. AUTOANTIBODIES AND SUICIDALITY

There are initial indications in addition to thyroid autoimmunity that suicidal behavior is a possible feature of autoantibody-mediated encephalitis (Kruse *et al*., 2015). There is evidence that older autoimmune encephalitis patients (Voltage gated potassium channel antibodies and striational muscle antibodies) suffered from increased psychopathology 12 months after the onset of AE, including increased suicidal ideation (Kruse *et al*., 2015). One study examined six different autoantibodies, in the CSF of patients who had attempted suicide. N-Methyl-D-Aspartate-Receptor, α-Amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA), gamma-aminobutyric acid B (GABAB), Leucin Rich Glioma Inactivated protein 1 (LGI1), contact associated protein 2 (CASPR2), and dipeptidyl-peptidase-like protein-6 (DPPX) were not detected in the CSF of 29 patients who had attempted suicide (Fernström *et al*., 2017). Although a higher CSF/serum albumin ratio was found in 5 patients, specific autoantibodies listed above were not identified (Fernström *et al*., 2017). These initial data confirm that autoantibodies against neural antigens probably play only minor role if any in suicidal behavior and are certainly not predictive of suicidal behavior.

CONCLUSIONS

Overall, our study results suggest that more proinflammatory than anti-inflammatory processes may be playing a role in suicide behavior. Nevertheless, it is important to emphasize that the association between individual biomarkers and suicidal behavior does not imply causality between such biomarkers and actual suicidal behavior. However, the evidence is solid that inflammatory biomarkers as characterized in Brundin's model (Brundin *et al*., 2017) can trigger suicidal behavior. There is also study evidence that patients with thyroid autoantibodies may also carry a higher risk of suicide, but this does not apply to the presence of neural autoantibodies. At the same time, what these studies make clear is the lack of large-scale investigations on this issue reflecting such an association from a wide range of neural autoantibodies. It is therefore important that such studies be conducted. We believe that various biomarkers of inflammation and immunological processes, including various neural autoantibodies, should therefore be investigated in patients with suicidal behavior. At the same time, however, we emphasize that no psychotherapeutic treatment strategies or personalized interventions for suicidal patients can be derived from our research results. To justify such a modified treatment approach, more research is needed in the field of biomarkers in suicidal patients. Furthermore, we stress that inflammation in the nervous system requires therapy such as autoimmune psychosis or psychiatric autoimmune encephalitis should be managed according to the currently recommended treatment pathways.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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