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Highlights

Saliva biomarkers in neurological disorders: A "spitting image" of brain health?

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ABSTRACT

In this issue of the *Biomedical Journal*, we learn how biomarkers in saliva may be able to provide insight into the health of the brain and the central nervous system. We also discover how computational modeling can help to identify potential epitopes for vaccine development against Chlamydia, the world's most common sexually transmitted infection.

Spotlight on reviews

Saliva biomarkers in neurological disorders: a "spitting image" of brain health?

The key to managing effectively the symptoms and limiting the progression of neurological diseases lies in early diagnosis. Yet, diagnosis remains challenging due to the complicated causes and manifestations of these diseases, and may involve invasive and painful tests like lumbar puncture. In this issue of the *Biomedical Journal*, Farah et al. [1] review a multitude of studies revealing that saliva may be a valuable source of biomarkers to facilitate early diagnosis of neurological diseases.

Saliva may appear pretty uninteresting but it is actually a complex liquid composed of various enzymes, hormones, antibodies, antimicrobial constituents, and growth factors [2]. All in all, your spit contains more than 2000 proteins, 27% of which are found in blood [3] and actually enter saliva directly from blood by passing through the space between cells [4]. Thus, saliva is functionally equivalent to serum in terms of reflecting the health status of the human body. It is also a lot easier to sample, with subjects being able to produce an ample supply, pain free and on demand (the average human actually produces somewhere between 1 and 1.5 L of the stuff every day). The feasibility of using saliva as a source of diagnostic biomarkers, "salivary diagnostics", has been examined for a whole host of diseases, including oral diseases, cancer, HIV, diabetes and cardiovascular diseases (reviewed in Ref. [5]).

But what can our saliva tell us about the health of our brain and the central nervous system? The answer, according to Farah et al. [1], fortunately appears to be quite a lot [Fig. 1]. Remarkably, even the proteins implicated in the pathological development of certain neurological diseases are capable of being detected in spit, and can hold vital information about diagnostics or disease status. Take for example alpha-synuclein (α-syn), the main constituent of Lewy bodies, which are the toxic protein clumps thought to lead the loss of dopaminergic and serotoninergic neurons in Parkinson's

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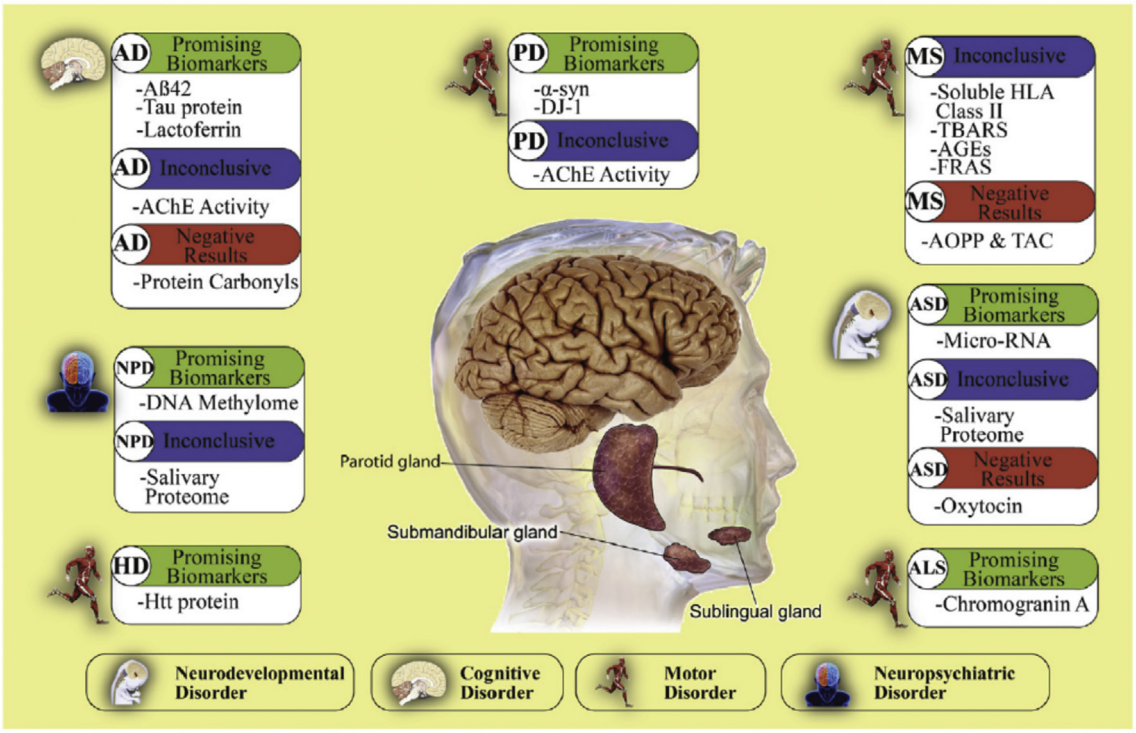

Fig. 1 The value of salivary biomarkers in neurological disorders. Biomarkers that may be useful for the diagnosis or prognosis of various neurological disorders are shown in green. Abbreviations used: AD : Alzheimer's disease; NPD : neuropsychiatric disorders; HD : Huntington's disease; PD : Parkinson's disease; MS : multiple sclerosis; ASD : autism spectrum disorder, ALS : amyotrophic lateral sclerosis. Figure kindly provided by Farah et al. [1]. See main article for more details on the various biomarkers.

disease (PD). When examining the concentration of α-syn in saliva, one study found that the proportion of the toxic oligomeric form of the protein was higher in patients with PD than in healthy controls [6]. Overall, levels of total α-syn in saliva are lower in patients with PD than in healthy controls, probably because of oligomerisation of free monomeric α-syn in the saliva of patients with PD, which reduces its total concentration [7,8]. Moreover, total levels of α-syn appear to correlate with disease severity in patients with PD, indicating its value not only as a diagnostic marker but also a prognostic one [6]. Similar to what is seen in PD, both huntingtin protein and amyloid beta peptides, the proteins implicated in Huntington's disease and Alzheimer's disease respectively, are capable of being detected in saliva and may be useful for diagnosis [9,10].

It is not just proteins however that offer insight into human health. Given that most neurological diseases are caused by a combination of genetic and environmental factors, much attention has turned to epigenetics – the array of mechanisms that regulate gene expression levels. Once such epigenetic mechanism is microRNA (miRNA), which are short non-coding RNA that interfere with gene expression by targeting complementary messenger RNA. In individuals with autism spectrum disorder (ASD), differences in the abundance of certain miRNA, compared to healthy controls, can be detected in post-mortem brain tissue [11]. Remarkably, such differences are also apparent in cells/tissues outside the brain, including olfactory mucosal stem cells [12] and saliva samples [13]. The target genes for the identified miRNAs were linked to neurodevelopment or had been previously associated with ASD. Clearly, there is a need to replicate these results, but they nonetheless offer the possibility of accelerating the detection of ASD, a spectrum of neurodevelopmental disorders that normally cannot be diagnosed before two years of age.

What works in the lab still has several barriers to face before it can be implemented in the clinic. A good diagnostic test must have high sensitivity and specificity, but also be high throughput, low cost and portable. The application of salivary diagnostics has seen rapid growth in recent years, with several emerging point-of-care-platforms allowing the analysis of various biomarkers (reviewed in Ref. [14]). With these developments, the key to early diagnosis of various neurological diseases could quite literally be on the tip of your tongue.

Spotlight on original articles

Epitope prediction: towards a Chlamydia *vaccine*

Chlamydia trachomatis is the world's most common sexually transmitted infection. Despite decades of research, there is still no vaccine against *C. trachomatis* approved for use in humans. In this issue of the *Biomedical Journal*, Russi et al. [15] hunt for B and T cell epitopes in a conserved pathogenic

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