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COMMENT

Response to "the role of the exposome in promoting resilience or susceptibility after SARS-CoV-2 infection"

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I read with interest the commentary from Pasinetti's group regarding the utility of the exposome paradigm for exploring environmental links to Covid-19 [1].

The authors propose a set of investigations to test hypotheses about connections between particular exposures—air pollutants, dietary fat, nicotine, and drugs—and the viral receptor for entry of SARS-CoV-2 into cells (ACE2). Such studies may produce scientific insights of importance to public health. However, they have no clear connection to "exposomics," which represent data-driven investigations for discovery of unknown causes of disease [2, 3]. Indeed, the hypotheses proposed by Naughton et al. can be pursued along traditional lines, and the authors cite early studies and case reports that have begun to do so.

By employing untargeted omics, exposomics generates hypotheses about potentially causal exposures or pathways that can be targeted for further investigation. In order to invoke exposomics for discovering environmental connections to Covid-19, one could take advantage of human blood that had been archived prior to diagnosis, from either prospective cohorts or routine clinical surveillance. These specimens would be probed with untargeted omics to measure myriad chemicals that collectively represent the "blood exposome," including small molecules (metabolomics and adductomics), large molecules (proteomics), metals (metallomics), and foreign DNA and RNA (metagenomics) [4]. By comparing abundances of these sets of omic features between Covid-19 cases and matched controls, discriminating species can be found. Targeted follow-up studies would then validate initial findings, confirm identities of discriminating features, explore environmental sources that give rise to these chemicals or the pathways they represent, and consider links with receptors, including ACE2. Although such a comprehensive exploration of the etiology of Covid-19 would take time, it could pay dividends by pinpointing hitherto unrecognized exposures from the diet, microbial metabolism, drugs, pollutants, other infections, and preexisting diseases that influence human risks from SARS-CoV-2 and related corona viruses.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

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