Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

NEWS Beyond Our Pages

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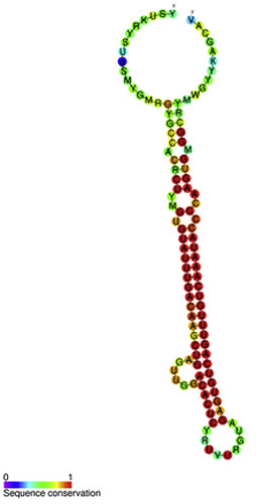
Recent advances in the fight against COVID-19

In response to the novel COVID-19 global pandemic, there has been a mass mobilization of the scientific community to find a cure. Gao et al (Science, https://doi.org/10.1126/science.abc1932) have recently developed an inactivated SARS-CoV-2 virus candidate vaccine that induced production of neutralizing antibodies against multiple strains in rodents and non-human primates and protected macaque monkeys against infection without evidence of antibody-dependent immune enhancement. Parallel efforts are ongoing to repurpose existing drugs and develop novel therapeutic agents effective against COVID-19. Wang et al (Lancet, https://doi.org/10.1016/S0140-6736(20)31022-9) determined that remdesivir, an inhibitor of replication of multiple classes of coronavirus, numerically reduced the time to clinical improvement in patients who began treatment within 10 days of symptom onset in a randomized controlled trial of patients with severe COVID-19. This result was not statistically significant; however, it should be noted that the trial was underpowered because it failed to reach the prespecified sample size. The NIH announced that a remdesivir clinical trial was stopped early as the drug was shown to accelerate recovery (from 15 to 11 days) and an early signal for improved clinical outcome was suggested (https://www.niaid.nih.gov/news-events/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19). Accordingly, the FDA issued an emergency use authorization for remdesivir, allowing the drug to be distributed and administered to treat suspected or laboratory-confirmed COVID-19 in adults and children hospitalized with severe disease.

In addition, Hung et al (Lancet, https://doi.org/10.1016/S0140-6736(20)31042-4) found in an open-label randomized trial in patients with mild-to-moderate COVID-19 that combined triple therapy with interferon beta-1b, lopinavir-ritonavir, and ribavirin decreased the duration of both viral shedding and hospital stay. To aid in identifying other potentially repurposable therapeutics, Gordon et al (Nature 2020 Apr 30. https://doi.org/10.1038/s41586-020-2286-9) characterized physical interactions between SARS-CoV-2 proteins and 66 human proteins known to be targeted by existing drugs. Importantly, antiviral activity was found *in vitro* in a subset of these compounds, including multiple inhibitors of mRNA translation. Finally, Abbott et al (Cell 2020 Apr 29. https://doi.org/10.1016/j.cell.2020.04.020) modulated CRISPR, a technique typically used for genome editing, to degrade SARS-CoV-2 RNA by targeting sequences conserved across multiple coronaviruses. Collectively, these findings highlight the exciting ongoing developments in the search for a cure for COVID-19.

MicroRNAs in asthma

Because several families of microRNAs have been associated with pathogenesis of asthma, Gomez et al (Am J Respir Crit Care Med 2020 Apr 7; https://doi.org/10.1164/rccm.201912-2360OC) performed a genome-wide analysis of microRNAs present in cells isolated from sputum. The authors identified 6 clusters of microRNAs that associated with clinical features of asthma. One particular cluster, whose expression positively correlated with sputum neutrophil and lymphocyte counts, was also associated with history of recurrent hospitalizations and impairment of lung function. The dominant miRNA within this cluster, *miR-223-3p*, was the most abundant neutrophil-derived microRNA that exerted downstream effects on the expression of genes associated with Toll-like receptor and T_H17 signaling. Overall, these results have furthered our understanding of the role of microRNAs in neutrophilic asthma and identify *miR-223-3p* as a potential therapeutic target worthy of further investigation. *Figure attribution: Public Domain at Wikimedia Commons by User Ppgardne / CC BY-SA (https://creativecommons.org/licenses/by-sa/3.0).*



Early life microbial exposures induce distinct asthma trajectories

Thysen et al (Sci Transl Med 2020 Feb 5;12(529); https://doi.org/10.1126/scitranslmed.aaw0258) performed extensive immune profiling of almost 200 parameters in 18-month old infants to determine the impact of early life microbial exposures on the development of asthma. Enhanced secretion of neutrophil-associated cytokines upon viral stimulation increased the risk of transient asthma at 6 years of age. In contrast, infants with enhanced IL-5

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and IL-13 production from stimulated T cells exhibited earlier airway bacterial colonization and increased development of persistent asthma by age 6. In total, the authors have demonstrated distinct immune responses early in life to microbial stimuli that selectively increase the risk for transient or persistent pediatric asthma.

Hans Bisgaard and Susanne Brix

We asked senior authors Hans Bisgaard, MD, DMSc, from Herlev and Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark, and Susanne Brix, MSc, PhD, from Technical University of Copenhagen in Lyngby, Denmark, to comment on the study. They write, "The study identifies the nature of deregulated immune responses to viruses or pathogenic airway bacteria in infants at risk of either transient or persistent asthma development. The data may pave the way for development of diagnostic tools for early diagnosis of the asthma endophenotype."

Local gastrointestinal IgE production in food allergy

Hoh et al (Sci Immunol 2020 Mar 6;5(45); http://doi.org/10.1126/sciimmunol.aay4209) utilized cutting-edge high-throughput DNA sequencing to characterize IgE-producing cells in mucosal tissues exposed to food antigens. IgE-expressing cells were found to be enriched in the stomach and duodenum and predominantly expressed a plasma cell phenotype. Additionally, some IgE-positive cells also co-expressed IgA, raising the possibility of local isotype class switching. Finally, similar antibody sequences directed against the peanut allergen Ara h 2 were found to be shared amongst different allergic patients. Collectively, these results show that the gastrointestinal tract is a potent reservoir of IgE-producing B cells in food allergy and suggest a possible role for common IgE gene rearrangements to its pathogenesis.

Exhaled nitric oxide is not predictive in mild asthma

Elevated blood eosinophil count and fraction of exhaled nitric oxide (FENO) predict increased risk of exacerbations and positive responses to inhaled corticosteroids in adult patients with severe asthma. In order to potentially extend these associations to mild asthma, Pavord et al (Lancet Respir Med 2020 Mar 11; https://doi.org/10.1016/S2213-2600(20)30053-9) performed a prespecified subgroup analysis of the previously reported Novel START randomized controlled trial (N Engl J Med 2019;380:2020-30; http://doi.org/10.1056/NEJMoa1901963) comparing either maintenance budesonide plus as-needed salbutamol or as-needed budesonide-formoterol to as-need salbutamol. Maintenance budesonide decreased the exacerbation rate only in subjects with high blood eosinophil counts. However, blood eosinophil count did not affect the response to as-needed budesonide-formoterol. Moreover, FENO levels did not affect the response to either inhaled corticosteroid treatment group. These results indicate that blood eosinophil count, but not FENO, predicts response to maintenance inhaled corticosteroids in mild asthma.

Ian D. Pavord

We asked first author Ian D. Pavord, MA DM FRCP FERS FMedSci from the University of Oxford in Oxford, United Kingdom to comment on the study. He writes, "Patients with higher blood eosinophils had a much higher rate of severe exacerbation if not randomized to an inhaled corticosteroid containing regime. Blood eosinophils are therefore a promising prognostic biomarker as well as predictive of response to inhaled corticosteroids."

Subcutaneous reslizumab is not effective in eosinophilic asthma

The anti-IL-5 antibody reslizumab has been approved with weight-based intravenous administration for use in patients with asthma with blood eosinophil counts of at least 400 cells/μL. Bernstein et al (Lancet Respir Med 2020 Feb 14; https://doi.org/10.1016/S2213-2600(19)30372-8) recently examined the efficacy of subcutaneous reslizumab in patients with severe asthma and blood eosinophil counts of at least 300 cells/μL. Subcutaneous reslizumab did not reduce the frequency of asthma exacerbations overall, although a benefit was seen in the subgroup of subjects with blood eosinophil counts greater than 400 cells/μL. Additionally, subcutaneous reslizumab did not decrease the daily maintenance glucocorticoid dose in patients with oral glucocorticoid-dependent asthma. The authors propose that the lower dose and systemic drug concentrations associated with fixed-dose subcutaneous administration likely are not sufficient for the full therapeutic effect. They also recommended accounting for regional differences in asthma exacerbation rates in future study designs.

Jonathan A. Bernstein

We asked first author Jonathan A. Bernstein, MD, from the University of Cincinnati College of Medicine in Cincinnati, Ohio, to comment on the study. He writes, "This study was undertaken to determine the efficacy of using a fixed dose of subcutaneous reslizumab in moderate-to-severe asthma patients. Although the primary endpoint of reducing asthma exacerbations and glucocorticoid daily dose was not significantly achieved, it was encouraging to see a significant improvement in reducing asthma exacerbations in a subgroup of patients with baseline eosinophils >300 cells/μL."

News items were written by medical writer Jared Travers, MD, PhD.