Capsule

Autism and mental retardation among offspring born after in vitro fertilization

Between 1978 and 2010, approximately 5 million infants were born after in vitro fertilization (IVF) treatments. Yet there is limited information on neurodevelopment after IVF, especially after the first year of life. Sandin et al. examine the association between use of any IVF and different IVF procedures and the risk of autistic disorder and mental retardation in the offspring. Of the more than 2.5 million infants born, 30,959 (1.2%) were conceived by IVF and were followed for a mean of 10 years (SD 6). Overall, 103 of 6959 children (1.5%) with autistic disorder and 180 of 15,830 (1.1%) with mental retardation were conceived by IVF. The relative risk for autistic disorder after any procedure compared with spontaneous conception was 1.14 (95% CI 0.94–1.39, 19.0 vs. 15.6 per 100,000 person-years). The RR for mental retardation was 1.18 (95% CI 1.01–1.36, 46.3 vs. 39.8 per 100,000 person-years). For both outcomes there was no statistically significant association when restricting analysis to singletons. Compared to IVF without ICSI with fresh embryo transfer, there were statistically significantly increased risks of autistic disorder following ICSI using surgically extracted sperm and fresh embryos (RR 4.60 [95% CI 2.14–9.88], 135.7 vs. 29.3 per 100,000 person-years); for mental retardation following ICSI using surgically extracted sperm and fresh embryos (RR 2.35 [95% CI 1.01–5.45], 144.1 vs. 60.8 per 100,000 person-years); and following ICSI using ejaculated sperm and fresh embryos (RR 1.47 [95% CI 1.03–2.09], 90.6 vs. 60.8 per 100,000 person-years). When restricting the analysis to singletons, the risks of autistic disorder associated with ICSI using surgically extracted sperm were not statistically significant, but the risks associated with ICSI using frozen embryos were significant for mental retardation (with frozen embryos, RR 2.36 [95% CI 1.04–5.36], 118.4 vs. 50.6 per 100,000 person-years]; with fresh embryos, RR 1.60 [95% CI 1.00–2.57], 80.0 vs. 50.6 per 100,000 person-years).

JAMA 2013; 310: 75

Eitan Israeli

Capsule

Fgf9 from dermal γδ T cells induces hair follicle neogenesis after wounding

Understanding molecular mechanisms for regeneration of hair follicles provides new opportunities for developing treatments for hair loss and other skin disorders. Gay et al. show that fibroblast growth factor 9 (Fgf9), initially secreted by γδ T cells, modulates hair follicle regeneration after wounding the skin of adult mice. Reducing Fgf9 expression decreases this wound-induced hair neogenesis (WIHN). Conversely, overexpression of Fgf9 results in a two- to threefold increase in the number of neogenic hair follicles. The authors found that Fgf9 from γδ T cells triggers Wnt expression and subsequent Wnt activation in wound fibroblasts. Through a unique feedback mechanism, activated fibroblasts then express Fgf9, thus amplifying Wnt activity throughout the wound dermis during a crucial phase of skin regeneration. Notably, humans lack a robust population of resident dermal γδ T cells, potentially explaining their inability to regenerate hair after wounding. These findings highlight the essential relationship between the immune system and tissue regeneration. The importance of Fgf9 in hair follicle regeneration suggests that it could be used therapeutically in humans.

Nature Med 2013; 19: 916

Eitan Israeli

Capsule

Topographic diversity of fungal and bacterial communities in human skin

Traditional culture-based methods have incompletely defined the microbial landscape of common recalcitrant human fungal skin diseases, including athlete's foot and toenail infections. Skin protects humans from invasion by pathogenic microorganisms and provides a home for diverse commensal microbiota. Bacterial genomic sequence data have generated novel hypotheses about species and community structures underlying human disorders. However, microbial diversity is not limited to bacteria; microorganisms such as fungi also have major roles in microbial community stability, human health and disease. Genomic methodologies to identify fungal species and communities have been limited compared with those that are available for bacteria. Fungal evolution can be reconstructed with phylogenetic markers, including ribosomal RNA gene regions and other highly conserved genes. Findley et al. sequenced and analyzed fungal communities of 14 skin sites in 10 healthy adults. Eleven core-body and arm sites were dominated by fungi of the genus Malassezia, with only species-level classifications revealing fungal community composition differences between sites. By contrast, three foot sites – plantar heel, toenail and toe web – showed high fungal diversity. Concurrent analysis of bacterial and fungal communities demonstrated that physiologic attributes and topography of skin differentially shape these two microbial communities. These results provide a framework for future investigation of the contribution of interactions between pathogenic and commensal fungal and bacterial communities to the maintenance of human health and to disease pathogenesis.

Nature 2013; 498: 367

Eitan Israeli

Capsule

Severe malaria is associated with parasite binding to endothelial protein C receptor

Sequestration of *Plasmodium falciparum*-infected erythrocytes in host blood vessels is a key triggering event in the pathogenesis of severe childhood malaria, which is responsible for about one million deaths every year. Sequestration is mediated by specific interactions between members of the *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) family and receptors on the endothelial lining. Severe childhood malaria is associated with expression of specific PfEMP1 subtypes containing domain cassettes (DCs) 8 and 13, but the endothelial receptor for parasites expressing these proteins was unknown. Turner et al. identified endothelial protein C receptor (EPCR), which mediates the cytoprotective effects of activated protein C, as the endothelial receptor for DC8 and DC13 PfEMP1. The authors show that EPCR binding is mediated through the amino-terminal cysteine-rich interdomain region (CIDRα1) of DC8 and group A PfEMP1 subfamilies, and that CIDRα1 interferes with protein C binding to EPCR. This PfEMP1 adhesive property links *P. falciparum* cytoadhesion to a host receptor involved in anticoagulation and endothelial cytoprotective pathways, and has implications for understanding malaria pathology and the development of new malaria interventions.

Nature 2013; 498: 502

Eitan Israeli

Capsule

Nucleation of platelets with blood-borne pathogens on Kupffer cells precedes other innate immunity and contributes to bacterial clearance

Through the use of intravital imaging of the liver, Wong et al. demonstrate a collaborative role for platelets with Kupffer cells (KCs) in eradicating blood-borne bacterial infection. Under basal conditions, platelets, via the platelet-adhesion receptor GPIb, formed transient 'touch-and-go' interactions with von Willebrand factor (vWF) constitutively expressed on KCs. Bacteria such as *Bacillus cereus* and methicillin-resistant *Staphylococcus aureus* (MRSA) were rapidly caught by KCs and triggered platelets to switch from 'touch-and-go' adhesion to sustained GPIIb-mediated adhesion on the KC surface to encase the bacterium. Infected GPIbα-deficient mice had more endothelial and KC damage than did their wild-type counterparts, which led to more fluid leakage, substantial polycythemia and rapid mortality. This study identifies a previously unknown surveillance mechanism by which platelets survey macrophages that rapidly converts to a critical host response to blood-borne bacteria.

Nature Immunol 2013; 14: 785

Eitan Israeli

Capsule

Hepatitis C virus infection activates an innate pathway involving IKK-α in lipogenesis and viral assembly

Hepatitis C virus (HCV) interacts extensively with host factors to not only establish productive infection but also trigger unique pathological processes. In a recent genome-wide siRNA screen Li and co-researchers demonstrated that IκB kinase-α (IKK-α) is a crucial host factor for HCV. Here they describe a new nuclear factor κB (NF-κB)-independent and kinase-mediated nuclear function of IKK-α in HCV assembly. HCV, through its 3' untranslated region, interacts with DEAD box polypeptide 3, X-linked (DDX3X) to activate IKK-α, which translocates to the nucleus and induces a CBP/p300-mediated transcriptional program involving sterol regulatory element-binding proteins (SREBPs). This innate pathway induces lipogenic genes and enhances core-associated lipid droplet formation to facilitate viral assembly. Chemical inhibitors of IKK-α suppress HCV infection and IKK-α–induced lipogenesis, offering a proof-of-concept approach for new HCV therapeutic development. These results show that HCV uses a novel mechanism to exploit intrinsic innate responses and hijack lipid metabolism, which may contribute to high chronicity rates and the pathological hallmark of steatosis in HCV infection.

Nature Med 2013; 19: 722

Eitan Israeli

Capsule

Vector transmission regulates immune control of Plasmodium virulence

Defining mechanisms by which Plasmodium virulence is regulated is central to understanding the pathogenesis of human malaria. Serial blood passage of Plasmodium through rodents, primates or humans increases parasite virulence, suggesting that vector transmission regulates Plasmodium virulence within the mammalian host. In agreement, disease severity can be modified by vector transmission, which is assumed to 'reset' Plasmodium to its original character. However, direct evidence that vector transmission regulates Plasmodium virulence is lacking. Spence et al. used mosquito transmission of serially blood passaged (SBP) *Plasmodium chabaudi chabaudi* to interrogate regulation of parasite virulence. Analysis of SBP *P. c. chabaudi* before and after mosquito transmission demonstrated that vector transmission intrinsically modifies the asexual blood-stage parasite, which in turn modifies the elicited mammalian immune response, which in turn attenuates parasite growth and associated pathology. Attenuated parasite virulence associates with modified expression of the *pir* multi-gene family. Vector transmission of Plasmodium therefore regulates gene expression of probable variant antigens in the erythrocytic cycle, modifies the elicited mammalian immune response, and thus regulates parasite virulence. These results place the mosquito at the center of our efforts to dissect mechanisms of protective immunity to malaria for the development of an effective vaccine.

Nature 2013; 498: 228

Eitan Israeli

Capsule

Exosomes mediate the cell-to-cell transmission of IFNα-induced antiviral activity

The cell-to-cell transmission of viral resistance is a potential mechanism for amplifying the interferon-induced antiviral response. In this study, Li et al. report that interferon-α (IFNα) induced the transfer of resistance to hepatitis B virus (HBV) from non-permissive liver non-parenchymal cells (LNPCs) to permissive hepatocytes via exosomes. Exosomes from IFNα-treated LNPCs were rich in molecules with antiviral activity. Moreover, exosomes from LNPCs were internalized by hepatocytes, which mediated the intercellular transfer of antiviral molecules. Finally, the authors found that exosomes also contributed to the antiviral response of IFNα to mouse hepatitis virus A59 and adenovirus in mice. Thus, they propose an antiviral mechanism of IFNα activity that involves the induction and intercellular transfer of antiviral molecules via exosomes.

Nature Immunol 2013; 14: 793

Eitan Israeli

Capsule

Tumor epigenetics

That human tumors display both genetic mutations and epigenetic alterations – for example, in DNA methylation – has been known for many years. With the completion of cancer genome sequencing projects, possible causal links between the two have come into sharper focus. The discovery of recurrent tumor-associated mutations in genes that encode chromatin-modifying enzymes or DNA methyltransferases represents a clear link between tumor genotype and "epigenotype." Emerging evidence suggests that a link can be subtle, as illustrated by two studies describing consistent epigenetic alterations in tumors with mutations in the gene encoding the metabolic enzyme succinate dehydrogenase (SDH). Killian et al. (*Cancer Discov* 2013; 3: 648) found that gastrointestinal stromal tumors harboring SDH mutations are characterized by dramatic and widespread DNA hypermethylation, whereas Letouzé et al. (*Cancer Cell* 2013; 23: 739) report that SDH-mutant paragangliomas display DNA hypermethylation that is associated with the silencing of genes involved in neuroendocrine cell differentiation. Both groups hypothesize that the hypermethylation phenotype is due to the aberrant accumulation of an oncometabolite that inhibits DNA-demethylating enzymes, with succinate being a strong candidate.

Eitan Israeli

Capsule

Inflammasome-derived IL-1β production induces nitric oxide-mediated resistance to Leishmania

Parasites of the Leishmania genus are the causative agents of leishmaniasis in humans, a disease that affects more than 12 million people worldwide. These parasites replicate intracellularly in macrophages, and the primary mechanisms underlying host resistance involve the production of nitric oxide (NO). In this study Lima-Junior et al. show that the Nlrp3 inflammasome is activated in response to Leishmania infection and is important for the restriction of parasite replication both in macrophages and in vivo as demonstrated through the infection of inflammasome-deficient mice with *Leishmania amazonensis*, *Leishmania braziliensis* and *Leishmania infantum chagasi*. Inflammasome-driven interleukin-1β (IL-1β) production facilitated host resistance to infection, as signaling through IL-1 receptor (IL-1R) and MyD88 was necessary and sufficient to trigger inducible nitric oxide synthase (NOS2)-mediated production of NO.

Nature Med 2013; 19: 909

Eitan Israeli

Capsule

De novo mutations in histone-modifying genes in congenital heart disease

Congenital heart disease (CHD) is the most frequent birth defect, affecting 0.8% of live births. Many cases occur sporadically and impair reproductive fitness, suggesting a role for de novo mutations. Zaidi et al. compare the incidence of de novo mutations in 362 severe CHD cases and 264 controls by analyzing exome sequencing of parent-offspring trios. CHD cases show a significant excess of protein-altering de novo mutations in genes expressed in the developing heart, with an odds ratio of 7.5 for damaging (premature termination, frameshift, splice site) mutations. Similar odds ratios are seen across the main classes of severe CHD. The authors find a marked excess of de novo mutations in genes involved in the production, removal or reading of histone 3 lysine 4 (H3K4) methylation, or ubiquitination of H2BK120, which is required for H3K4 methylation. There are also two de novo mutations in *SMAD2*, which regulates H3K27 methylation in the embryonic left-right organizer. The combination of both activating (H3K4 methylation) and inactivating (H3K27 methylation) chromatin marks characterizes 'poised' promoters and enhancers, which regulate expression of key developmental genes. These findings implicate de novo point mutations in several hundreds of genes that collectively contribute to approximately 10% of severe CHD.

Nature 2013; 498: 220

Eitan Israeli

Capsule

Inflammatory monocytes regulate pathologic responses to commensals during acute gastrointestinal infection

The commensal flora can promote both immunity to pathogens and mucosal inflammation. How commensal-driven inflammation is regulated in the context of infection remains poorly understood. Grainger et al. show that during acute mucosal infection of mice with *Toxoplasma gondii*, inflammatory monocytes acquire a tissue-specific regulatory phenotype associated with production of the lipid mediator prostaglandin E2 (PGE2). Notably, in response to commensals, inflammatory monocytes can directly inhibit neutrophil activation in a PGE2-dependent manner. Further, in the absence of inflammatory monocytes, mice develop severe neutrophil-mediated pathology in response to pathogen challenge that can be controlled by PGE2 analog treatment. Complementing these findings, inhibition of PGE2 led to enhanced neutrophil activation and host mortality after infection. These data demonstrate a previously unappreciated dual action of inflammatory monocytes in controlling pathogen expansion while limiting commensal-mediated damage to the gut. These results place inflammatory monocyte-derived PGE2 at the center of a commensal-driven regulatory loop required to control host-commensal dialog during pathogen-induced inflammation.

Nature Med 2013; 19: 713

Eitan Israeli

Capsule

Bacillus thuringiensis (Bt) toxin to combat worms

Some humans share several characteristics with pigs, including very similar parasitic worms. Ascaris spp. roundworms are large and pungent, and can occur in sufficient numbers to block the gut, pierce the peritoneum, and invade the bile duct. In children, the morbidity caused by a heavy worm infection can have lifelong consequences. Surprisingly perhaps, roundworms can be killed by a *Bacillus thuringiensis* (Bt) toxin, a bacterium more usually encountered in crop pest control. Urban et al. have been exploring the potential of one Bt toxin, Cry5B, as an anthelmintic (a deworming drug), using young pigs as a human substitute. Experiments on the mode of action in the classic worm model *Caenorhabditis elegans* showed that Cry5B binds to galactose-containing glycolipid receptors found only in invertebrates, and this was confirmed to be the case in Ascaris too. Cry5B was given by gavage to groups of five piglets as spore crystal lysate in two doses (20 mg/kg) 10 and 12 days after infection, when the penultimate larval worm stage emerges into the gut (unfortunately, there are severe practical constraints on testing the limited-availability Bt toxin on the slow-growing adult worms), and 6 days later 97% of these larvae were dead and the remainder disabled. The natural product Cry5B could thus be a valuable addition to the anthelmintic roster, especially as resistance is emerging to the standard drugs.

PLoS Negl Trop Dis 2013; 7: e2263

Eitan Israeli

Capsule

Biological features of a novel avian influenza A (H7N9) virus

Human infection associated with a novel reassortant avian influenza H7N9 virus has recently been identified in China. A total of 132 confirmed cases and 39 deaths have been reported. Most patients presented with severe pneumonia and acute respiratory distress syndrome. Although the first epidemic has subsided, the presence of a natural reservoir and the disease severity highlight the need to evaluate its risk on human public health and to understand the possible pathogenesis mechanism. Zhou et al. show that the emerging H7N9 avian influenza virus poses a potentially high risk to humans. The authors discovered that the H7N9 virus can bind to both avian-type (α2,3-linked sialic acid) and human-type (α2,6-linked sialic acid) receptors. It can invade epithelial cells in the human lower respiratory tract and type II pneumonocytes in alveoli, and replicate efficiently in ex vivo lung and trachea explant culture and several mammalian cell lines. In acute serum samples of H7N9-infected patients, increased levels of the chemokines and cytokines IP-10, MIG, MIP-1β, MCP-1, IL-6, IL-8 and IFNα were detected. They note that the human population is naive to the H7N9 virus, and current seasonal vaccination could not provide protection.

Nature 2013; doi:10.1038/*nature12379*

Eitan Israeli

Capsule

Regulatory T cells protect the gut

Regulatory T cells (Tregs) in the gut are important sentinels in maintaining the peace between our gut and its trillions of resident bacteria and have been shown to be regulated by specific strains of bacteria in mouse models. Smith and collaborators question whether metabolite(s) generated by resident bacterial species may regulate Tregs in the gut. Indeed, short-chain fatty acids (SCFAs), bacterial fermentation products of dietary fibers produced by a range of bacteria, restored colonic Treg numbers in mice devoid of a gut microbiota and increased Treg numbers in colonized mice. The effects of SCFAs on Tregs were mediated through GPCR43, a receptor for SCFAs, which is expressed on colonic Tregs. Mice fed SCFAs were protected against experimentally induced colitis in a manner that was dependent on GPR43-expressing Tregs.

Science 2013; 341: 569

Eitan Israeli

Capsule

CD36 coordinates NLRP3 inflammasome activation by facilitating intracellular nucleation of soluble ligands into particulate ligands in sterile inflammation

Particulate ligands, including cholesterol crystals and amyloid fibrils, induce production of interleukin 1β (IL-1β) dependent on the cytoplasmic sensor NLRP3 in atherosclerosis, Alzheimer's disease and diabetes. Soluble endogenous ligands, including oxidized low density lipoprotein (LDL), amyloid-β and amylin peptides, accumulate in such diseases. Sheedy and team identified an endocytic pathway mediated by the pattern-recognition receptor CD36 that coordinated the intracellular conversion of those soluble ligands into crystals or fibrils, which resulted in lysosomal disruption and activation of the NLRP3 inflammasome. Consequently, macrophages that lacked CD36 failed to elicit IL-1β production in response to those ligands, and targeting CD36 in atherosclerotic mice resulted in lower serum concentrations of IL-1β and accumulation of cholesterol crystals in plaques. Collectively, these findings highlight the importance of CD36 in the accrual and nucleation of NLRP3 ligands from within the macrophage and position CD36 as a central regulator of inflammasome activation in sterile inflammation.

Nature Immunol 2013; 14: 812

Eitan Israeli

Capsule

Autism-specific maternal autoantibodies recognize critical proteins in the developing brain

Autism spectrum disorders (ASDs) are neurodevelopmental in origin, affecting an estimated 1 in 88 children in the United States. Braunschweig and colleagues previously described ASD-specific maternal autoantibodies that recognize fetal brain antigens. Now they demonstrate that lactate dehydrogenase A and B (LDH), cypin, stress-induced phosphoprotein 1 (STIP1), collapsin response mediator proteins 1 and 2 (CRMP1, CRMP2) and Y-box-binding protein comprise the seven primary antigens of maternal autoantibody-related (MAR) autism. Exclusive reactivity to specific antigen combinations was noted in 23% of mothers of ASD children and only 1% of controls. ASD children from mothers with specific reactivity to LDH, STIP1 and CRMP1 and/or cypin (7% vs. 0% in controls, $P < 0.0002$, odds ratio 24.2, 95% confidence interval 1.45–405) had elevated stereotypical behaviors compared with ASD children from mothers lacking these antibodies. The authors describe the first panel of clinically significant biomarkers with over 99% specificity for autism risk, thereby advancing our understanding of the etiologic mechanisms and therapeutic possibilities for MAR autism.

Translational Psychiatry 2013; 3: e277

Eitan Israeli

Capsule

Preclinical study on cell therapy for mitigation of lethal acute radiation response by Hadassah research group is published in *PLOS ONE*

Prof. Raphael Gorodetsky and his team in the Biotechnology and Radiobiology Laboratory of the Sharett Institute of Oncology at Hadassah Hospital report a breakthrough cell-therapy study for mitigation of lethal acute radiation syndrome (ARS) by simple intramuscular injection of human placental stromal cells. This preclinical study was performed with specific composition of 3D expanded allogeneic cells (PLX-RAD) produced by Pluristem (Haifa), which were found by the researchers to be most effective for this application. The results suggest an "off the shelf" safe therapy to mitigate ARS by a simple intramuscular injection of the placental cell preparations with minimal anticipated adverse effect or complications. The immediate clinical application of this study is for scenarios of nuclear disasters, where large populations may be exposed to high doses of ionizing radiation with no accurate individual dose estimation. The treatment is practical in such events since its initiation could be delayed for at least by 1–2 days. The authors suggest that their findings may also be applied in clinical practice for bone marrow failure and pancytopenia.

PLOS ONE http://dx.plos.org/10.1371/journal.pone.0066549

Capsule

Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome

Obesity has become more prevalent in most developed countries over the past few decades, and is increasingly recognized as a major risk factor for several common types of cancer. As the worldwide obesity epidemic has shown no signs of abating, better understanding of the mechanisms underlying obesity-associated cancer is urgently needed. Although several events were proposed to be involved in obesity-associated cancer, the exact molecular mechanisms that integrate these events have remained largely unclear. Yoshimoto and co-researchers show that senescence-associated secretory phenotype (SASP) plays a crucial role in promoting obesity-associated hepatocellular carcinoma (HCC) development in mice. Dietary or genetic obesity induces alterations of gut microbiota, thereby increasing the levels of deoxycholic acid (DCA), a gut bacterial metabolite known to cause DNA damage. The enterohepatic circulation of DCA provokes SASP phenotype in hepatic stellate cells (HSCs), which in turn secrete various inflammatory and tumor-promoting factors in the liver, thus facilitating HCC development in mice after exposure to chemical carcinogen. Notably, blocking DCA production or reducing gut bacteria efficiently prevents HCC development in obese mice. Similar results were also observed in mice lacking an SASP inducer or depleted of senescent HSCs, indicating that the DCA–SASP axis in HSCs has key roles in obesity-associated HCC development. Moreover, signs of SASP were also observed in the HSCs in the area of HCC arising in patients with non-alcoholic steatohepatitis, indicating that a similar pathway may contribute to at least certain aspects of obesity-associated HCC development in humans as well. These findings provide valuable new insights into the development of obesity-associated cancer and open up new possibilities for its control.

Nature 2013; 499: 97

Eitan Israeli

Capsule

USA tries to tighten exemptions from mandatory vaccinations

In the United States, states have the authority to grant exemptions so that children can begin to attend school without having been vaccinated against childhood diseases. Medical exemptions can be granted when a child has a history of allergic reactions or is immunocompromised. However, there has been a noticeable increase in the numbers of unvaccinated children resulting from non-medical exemptions, based on religious or philosophical grounds; in 2011–2012, roughly 80% of all exemptions were non-medical. Blank et al. have gathered information from public health officials, health departments, the Centers for Disease Control and Prevention, the National Conference of State Legislatures, and state legislature databases. Policies were characterized as easy, medium, or difficult, according to the level of effort they would pose for parents requesting exemptions. The lower the barrier, the more non-medical exemptions were observed, with a twofold difference between the easiest and most difficult procedures. For 2011–2012, at least 21 bills were introduced at the state level to change the exemption procedures, and exemptions would have been made easier if bills in 10 states had passed. As of February 2013, three bills have been introduced in two states to tighten exemptions, and five bills have been introduced in four states to loosen them. The authors advocate social and policy efforts to promote parental education and to stem the spread of vaccine-preventable diseases.

Health Affairs 2013; 32: 1282

Eitan Israeli

Capsule

Arab Muslin heads Emergency Medicine at Hadassah

Dr. Aziz Darawshe, former head of emergency medicine at HaEmek Medical Center in Afula, was recently appointed director of Emergency Medicine at Hadassah University Medical Center in Jerusalem (Ein Kerem campus) Darawshe earned his reputation for medical excellence while working at HaEmek, where consumer satisfaction polls performed by Clalit Health Services rated his team among the best. An oasis for Jewish-Arab coexistence, almost 40% of the medical staff at HaEmek is Arab and the staff work together without discrimination and regardless of the political situation. According to Darawshe, "The integration of Arabs in to the medical field has been impressive in this country. In the health system, Arabs and Jews get along excellently on an individual level. It's an oasis. Since the establishment of the State of Israel, this has been so in hospitals and health funds and in Education Ministry institutions. The rate of Arab pharmacists is about 40%."

Darwashe studied medicine at the University of Sofia in Bulgaria, specializing in cardiology, emergency medicine and internal medicine. He also possesses a masters' degree in health management systems from Ben-Gurion University of the Negev. Additionally, since 2010, he has served as chairman of the Israel Society for Urgent Medicine, and as of 2011 is an honorary member of the American College of Emergency Physicians. From a family with little education, his parents prioritized a better future for their children – Aziz's siblings include three physicians, a dentist, an engineer, and five sisters with academic degrees. His eldest son has a medical degree from Jerusalem. Known as a political moderate, Darawshe believes that by healing the sick, without discriminating based on nationality, coexistence is possible.

With thanks to Rachel Avraham