Capsule

Integration of adult-born brain cells

Physical exercise or exploration of a novel environment greatly influences the production, maturation, and connectivity of adult-born neurons. Alvarez and co-authors investigated how experience affects the incorporation of adult-born neurons into the hippocampal network. A brief period of sensory enrichment when new neurons were 9 to 10 days old led to neurons having larger dendrites and more functional spine synapses. A disynaptic preexisting feedback circuit promoted the growth and integration of the new cells.

Science 2016; 354: 459

Eitan Israeli

Capsule

Inhibition of HDAC8 and HDAC9 by microbial short-chain fatty acids breaks immune tolerance of the epidermis to TLR ligands

Epidermal keratinocytes participate in immune defense through their capacity to recognize danger, trigger inflammation, and resist infection. However, normal skin immune function must tolerate contact with an abundant community of commensal microbes without inflammation. Sanford and team hypothesized that microbial environmental conditions dictate the production of molecules that influence epigenetic events and cause keratinocytes to break innate immune tolerance. *Propionibacterium acnes*, a commensal skin bacterium, produced the short-chain fatty acids (SCFAs) propionate and valerate when provided a lipid source in hypoxic growth conditions, and these SCFAs inhibited histone deacetylase (HDAC) activity. Inhibition of HDAC activity in keratinocytes promoted cytokine expression in response to Toll-like receptor (TLR) ligands for TLR2 or TLR3. This response was opposite to the action of HDAC inhibition on production of inflammatory cytokines by monocytes and involved HDAC8 and HDAC9 because small interfering RNA silencing of these HDACs recapitulated the activity of SCFAs. Analysis of cytokine expression in mice confirmed the response of the epidermis where application of SCFA on the skin surface promoted cytokine expression, whereas subcutaneous administration was inhibitory. These findings show that the products of commensal microbes made under specific conditions will inhibit HDAC activity and break tolerance of the epidermis to inflammatory stimuli.

Sci Immunol 2016: 1: doi: 10.1126/sciimmunol.aah4609

Eitan Israeli

Capsule

Transmission of *Babesia microti* parasites by solid organ transplantation

Babesia microti, an intra-erythrocytic parasite, is tickborne in nature. In contrast to transmission by blood transfusion, which has been well documented, transmission associated with solid organ transplantation has not been reported. Brennan et al. describe parasitologically confirmed cases of babesiosis diagnosed about 8 weeks post-transplantation in two recipients of renal allografts from an organ donor who was multiply transfused on the day he died from traumatic injuries. The organ donor and recipients had no identified risk factors for tickborne infection. Antibodies against *B. microti* parasites were not detected by serologic testing of archived pre-transplant specimens. However, one of the organ donor's blood donors was seropositive when tested post-donation and had risk factors for tick exposure. The organ donor probably served as a conduit of *Babesia* parasites from the seropositive blood donor to both kidney recipients. Babesiosis should be included in the differential diagnosis of unexplained fever and hemolytic anemia after blood transfusion or organ transplantation.

Emerg Infect Dis 2016; 22: 1869

Eitan Israeli

Capsule

Fulminant myocarditis with combination immune checkpoint blockade

Immune checkpoint inhibitors have improved clinical outcomes associated with numerous cancers, but high grade, immune related adverse events can occur, particularly with combination immunotherapy. Johnson et al. report the cases of two patients with melanoma in whom fatal myocarditis developed after treatment with ipilimumab and nivolumab. In both patients, there was development of myositis with rhabdomyolysis, early progressive and refractory cardiac electrical instability, and myocarditis with a robust presence of T cell and macrophage infiltrates. Selective clonal T cell populations infiltrating the myocardium were identical to those present in tumors and skeletal muscle. Pharmacovigilance studies show that myocarditis occurred in 0.27% of patients treated with a combination of ipilimumab and nivolumab, which suggests that our patients were having a rare, potentially fatal, T cell-driven drug reaction.

N Engl J Med 2016; 375: 1749

Eitan Israeli

Capsule

Ribociclib as first-line therapy for HR-positive, advanced breast cancer

The inhibition of cyclin-dependent kinases 4 and 6 (CDK4/6) could potentially overcome or delay resistance to endocrine therapy in advanced breast cancer that is positive for hormone receptor (HR) and negative for human epidermal growth factor receptor 2 (HER2). Hortobagyu et al. found that the duration of progression-free survival was significantly longer in the ribociclib group than in the placebo group (hazard ratio 0.56, 95%CI 0.43–0.72, $P = 3.29 \times 10^{-6}$ for superiority). The median duration of follow-up was 15.3 months. After 18 months, the progression-free survival rate was 63.0% (95%CI 54.6–70.3) in the ribociclib group and 42.2% (95%CI 34.8–49.5) in the placebo group. In patients with measurable disease at baseline, the overall response rate was 52.7% and 37.1%, respectively ($P < 0.001$). Common grade 3 or 4 adverse events that were reported in more than 10% of the patients in either group were neutropenia (59.3% in the ribociclib group vs. 0.9% in the placebo group) and leukopenia (21.0% vs. 0.6%); the rates of discontinuation because of adverse events were 7.5% and 2.1%, respectively.

N Engl J Med 2016; 375: 1738

Eitan Israeli

"The color of truth is grey"

Andre Gide (1869-1951), French writer and Nobel laureate

Capsule

Airplane air affects jet leg

Can flying help alleviate jet lag? Studies of the biochemical mechanisms that synchronize biological clocks throughout the body show that the low oxygen environment of airplanes may actually help you adjust to your new time zone. Adamovich et al. observed daily cycles in the concentration of oxygen in blood and tissues of mice kept on a normal light-dark cycle. These variations were sufficient to alter the abundance of the transcription factor HIF1α (hypoxia-inducible factor 1α). In cultured cells, changes in oxygen concentration could entrain the circadian clock only if HIF1α was present. When animals were subjected to a 6 hour change in the light cycle (like traveling eastward on a jet), animals kept in a low concentration of oxygen adapted more quickly.

Cell Metab 2016; 10.1016/j.cmet.2016.09.014

Eitan Israeli

Capsule

Type I interferon suppresses virus-specific B cell responses by modulating CD8+ T cell differentiation

Studies have established a role for T cells in resolving persistent viral infections, yet emerging evidence indicates that both T and B cells are required to control some viruses. During persistent infection, a marked lag or failure to generate neutralizing antibodies is commonly observed and likely contributes to an inability to control certain pathogens. Using lymphocytic choriomeningitis virus (LCMV) as a model, Moseman et al. examined how a persistent viral infection can suppress neutralizing humoral immunity. By tracking the fate of virus-specific B cells in vivo, the authors report that LCMV-specific B cells were rapidly deleted within a few days of persistent infection, and this deletion was completely reversed by blockade of type I interferon (IFN-I) signaling. Early interference with IFN-I signaling promoted survival and differentiation of LCMV-specific B cells, which accelerated the generation of neutralizing antibodies. This marked improvement in antiviral humoral immunity did not rely on the cessation of IFN-I signaling in B cells but on alterations in the virus-specific CD8+ T cell response. Using two-photon microscopy and in vivo calcium imaging, they observed that cytotoxic T lymphocytes (CTLs) productively engaged and killed LCMV-specific B cells in a perforin-dependent manner within the first few days of infection. Blockade of IFN-I signaling protected LCMV-specific B cells by promoting CTL dysfunction. Therapeutic manipulation of this pathway may facilitate efforts to promote humoral immunity during persistent viral infection in humans. These findings illustrate how events that occur early after infection can disturb the resultant adaptive response and contribute to viral persistence.

Sci Immunol 2016; 1: doi: 10.1126/sciimmunol.aah3565

Eitan Israeli

"You may shoot me with your words
You may cut me with your eyes
You may kill me with your hatefulness
But still, like air, I'll rise"

Maya Angelou (1928-2014), American poet and civil rights activist

Capsule

Lifelong protection against severe influenza

The first influenza attack that a child suffers can affect the way that their lifelong immunity to the virus builds up. A wide range of influenza A virus subtypes infect humans. Subtype H5 belongs to HA group 1 (which also includes H1 and H2 subtypes), and subtype H7 belongs to HA group 2 (which also includes the H3 subtype). Gostic et al. found that birth-year cohorts that experienced first infections with seasonal H3 subtype viruses were less susceptible to the potentially fatal avian influenza H7N9 virus. Conversely, older individuals who were exposed to H1 or H2 subtype viruses as youngsters were less susceptible to avian H5N1-bearing viruses. A mathematical model of the protective effect of this imprinting could potentially prove useful to predict the age distribution and severity of future pandemics.

Science 2016; 354: 722

Eitan Israeli

Capsule

A new direction for breast cancer therapy

Triple-negative breast cancer has the worst prognosis of the breast cancer subtypes. Aggressive forms of this cancer show elevated signaling through the transcription factor MYC, but blocking MYC activity remains challenging because of its role in normal cell function. Horiuchi et al. screened the protein kinases expressed by triple-negative breast tumors in hopes of finding a way to thwart MYC indirectly. They identified PIM1, a non-essential protein kinase that was highly active in MYC-positive tumors. Genetic depletion of PIM1 promoted cancer cell death, and preclinical drugs targeting PIM1 impaired the growth of MYC-positive patient tumors in mice. These findings pave the way for the development of PIM1 inhibitors in early-phase clinical trials.

Nat Med 2016; 10.1038/nm.4213

Eitan Israeli

Capsule

Caspase-2 cleavage of tau reversibly impairs memory

In Alzheimer's disease (AD) and other tauopathies, the tau protein forms fibrils, which are believed to be neurotoxic. However, fibrillar tau has been dissociated from neuron death and network dysfunction, suggesting the involvement of non-fibrillar species. Zhao and fellow-researchers describe a novel pathological process in which caspase-2 cleavage of tau at Asp314 impairs cognitive and synaptic function in animal and cellular models of tauopathies by promoting the missorting of tau to dendritic spines. The truncation product, Δtau314, resists fibrillation and is present at higher levels in brains from cognitively impaired mice and humans with AD. The expression of tau mutants that resisted caspase-2 cleavage prevented tau from infiltrating spines, dislocating glutamate receptors and impairing synaptic function in cultured neurons, and it prevented memory deficits and neurodegeneration in mice. Decreasing the levels of caspase-2 restored long-term memory in mice that had existing deficits. These results suggest an overall treatment strategy for re-establishing synaptic function and restoring memory in patients with AD by preventing tau from accumulating in dendritic spines.

Nature Med 2016; 22: 1268

Eitan Israeli

"If you light a fire for others, it will also brighten one's own way"

13th century Buddhist sage

Capsule

Hyaluronan and TLR4 promote surfactant-protein C-positive alveolar progenitor cell renewal and prevent severe pulmonary fibrosis in mice

Successful recovery from lung injury requires the repair and regeneration of alveolar epithelial cells to restore the integrity of gas-exchanging regions within the lung and preserve organ function. Improper regeneration of the alveolar epithelium is often associated with severe pulmonary fibrosis, the latter of which involves the recruitment and activation of fibroblasts, as well as matrix accumulation. Type 2 alveolar epithelial cells (AEC2s) are stem cells in the adult lung that contribute to the lung repair process. The mechanisms that regulate AEC2 renewal are incompletely understood. Liang et al. provide evidence that expression of the innate immune receptor Toll-like receptor 4 (TLR4) and the extracellular matrix glycosaminoglycan hyaluronan (HA) on AEC2s are important for AEC2 renewal, repair of lung injury and limiting the extent of fibrosis. Either deletion of TLR4 or HA synthase 2 in surfactant-protein C-positive AEC2s leads to impaired renewal capacity, severe fibrosis and mortality. Furthermore, AEC2s from patients with severe pulmonary fibrosis have reduced cell surface HA and impaired renewal capacity, suggesting that HA and TLR4 are key contributors to lung stem cell renewal and that severe pulmonary fibrosis is the result of distal epithelial stem cell failure.

Nature Med 2016; 22: 1285

Eitan Israeli

Capsule

How macrophages build a wall

Granulomas are a defining feature of infection with *Mycobacterium tuberculosis*, the causative agent of tuberculosis. Macrophages are the primary component of these cell structures, which are thought to protect the host by walling off the pathogen. Cronan et al. studied granulomas in optically transparent zebrafish infected with *M. marinum* to directly visualize how they form. They observed that macrophages in granulomas undergo epithelial reprogramming, up-regulating many molecules and adhesion structures characteristic of epithelial cells. Disrupting this process by blocking E-cadherin, a protein that drives the epithelialization process, led to granulomas with a disorganized appearance. Unexpectedly, however, this reduced the fishes' bacterial burden, suggesting that granulomas may not always be host-protective.

Immunity 2016; 45: 861

Eitan Israeli

Capsule

British squirrels infected with leprosy

With the exception of armadillos in the Americas, leprosy infections are considered almost exclusively restricted to humans. Avanzi and team examined warty growths on the faces and extremities of red squirrels in the British Isles and found that two species of leprosy-causing organisms were to blame. *Mycobacterium leprae* in the southern population of Brownsea Island squirrels originated from a medieval human strain. *M. lepromatosis* was found in red squirrels from elsewhere in the United Kingdom and Ireland. Human leprosy is proving hard to eradicate, despite available drugs. Perhaps other wildlife species are also reservoirs for this stubborn disease.

Science 2016; 354: 744

Eitan Israeli

"I have not failed. I've just found 10,000 ways that won't work"

Thomas A. Edison (1847-1931), American inventor and businessman, who developed many devices that greatly influenced life around the world, including the phonograph, the motion picture camera, and the long-lasting, practical electric light bulb. He was one of the first inventors to apply the principles of mass production and large-scale teamwork to the process of invention and is thus credited with the creation of the first industrial research laboratory

Capsule

Aggregation by design

Amyloid aggregation is driven by short sequences within proteins that self-assemble into characteristic amyloid structures. About 30 human proteins are implicated in amyloid-associated diseases, but many more contain short sequences that are potentially amyloidogenic. Gallardo and colleagues designed a peptide based on an amyloidogenic sequence in the vascular endothelial growth factor receptor VEGFR2. The peptide induced VEGFR2 to form aggregates with features characteristic of amyloids. Amyloids were toxic only in cells that required VEGFR2 activity, suggesting that the toxicity was due to loss of function of VEGFR2, rather than to inherent toxicity of the aggregates. The peptide inhibited VEGFR2-dependent tumor growth in a mouse tumor model.

Science 2016; 354: 10.1126/*science*.aah4949

Eitan Israeli

Capsule

Global spread of aggressive mycobacteria

Many mycobacteria, in addition to those causing leprosy and tuberculosis, are capable of infecting humans. Some can be particularly dangerous in patients suffering from immunosuppression or chronic disease, such as cystic fibrosis (CF). Bryant and group observed clusters of near-identical isolates of drug-resistant *Mycobacterium abscessus* in patients reporting to CF clinics. The similarity of the isolates suggests transmission between patients, rather than environmental acquisition. Although this bacterium is renowned for its environmental resilience, the mechanism for its long-distance transmission among the global CF patient community remains a puzzle.

Science 2016; 354: 751

Eitan Israeli

Capsule

A look at early multiple sclerosis

In multiple sclerosis and similar diseases in animals, the brain becomes inflamed, which ultimately causes neurons to degenerate. Gerwien et al. found two protein-degrading enzymes that are absolutely required for this process: MMP-2 and MMP-9. MMP-9 resides in immune cells and is required for the entry of these cells into the brain as the disease begins. The authors developed tools to visualize MMP inhibitors at this initial stage of multiple sclerosis and its mouse equivalent, just as immune cells began their inflammatory infiltration of the brain.

Sci Transl Med 2016; 8: 364ra152

Eitan Israeli

Capsule

PIM1 kinase regulates cell death, tumor growth and chemotherapy response in triple-negative breast cancer

Triple-negative breast cancers (TNBCs) have poor prognosis and lack targeted therapies. Braso-Maristany et al. identified increased copy number and expression of the *PIM1* proto-oncogene in genomic data sets of patients with TNBC. TNBC cells, but not non-malignant mammary epithelial cells, were dependent on PIM1 for proliferation and protection from apoptosis. *PIM1* knockdown reduced expression of the anti-apoptotic factor BCL2, and dynamic BH3 profiling of apoptotic priming revealed that PIM1 prevents mitochondrial-mediated apoptosis in TNBC cell lines. In TNBC tumors and their cellular models, *PIM1* expression was associated with several transcriptional signatures involving the transcription factor MYC, and PIM1 depletion in TNBC cell lines decreased, in a MYC-dependent manner, cell population growth and expression of the MYC target gene MCL1. Treatment with the pan-PIM kinase inhibitor AZD1208 impaired the growth of both cell line and patient-derived xenografts and sensitized them to standard-of-care chemotherapy. This study identified PIM1 as a malignant cell-selective target in TNBC and the potential use of PIM1 inhibitors for sensitizing TNBC to chemotherapy-induced apoptotic cell death.

Nature Med 2016; 22: 1303

Eitan Israeli

Capsule

Determinants of HIV-1 broadly neutralizing antibody induction

Broadly neutralizing antibodies (bnAbs) are a focal component of HIV-1 vaccine design, yet basic aspects of their induction remain poorly understood. Rusert et al. report on viral, host and disease factors that steer bnAb evolution using the results of a systematic survey in 4,484 HIV-1-infected individuals that identified 239 bnAb inducers. The authors show that three parameters that reflect the exposure to antigen – viral load, length of untreated infection and viral diversity – independently drive bnAb evolution. Notably, black participants showed significantly (P = 0.0086–0.038) higher rates of bnAb induction than white participants. Neutralization fingerprint analysis, which was used to delineate plasma specificity, identified strong virus subtype dependencies, with higher frequencies of CD4-binding-site bnAbs in infection with subtype B viruses (P = 0.02) and higher frequencies of V2-glycan-specific bnAbs in infection with non-subtype B viruses ($P = 1 \times 10^{-5}$). Thus, key host, disease and viral determinants, including subtype-specific envelope features that determine bnAb specificity, remain to be unraveled and harnessed for bnAb-based vaccine design.

Nature Med 2016; 22: 1260

Eitan Israeli

Capsule

Transplanted embryonic neurons integrate into adult neocortical circuits

The ability of the adult mammalian brain to compensate for neuronal loss caused by injury or disease is very limited. Transplantation aims to replace lost neurons, but the extent to which new neurons can integrate into existing circuits is unknown. Using chronic in vivo two-photon imaging, Falkner et al. show that embryonic neurons transplanted into the visual cortex of adult mice mature into bona fide pyramidal cells with selective pruning of basal dendrites, achieving adult-like densities of dendritic spines and axonal boutons within 4–8 weeks. Monosynaptic tracing experiments reveal that grafted neurons receive area-specific afferent inputs matching those of pyramidal neurons in the normal visual cortex, including topographically organized geniculo-cortical connections. Furthermore, stimulus-selective responses refine over the course of many weeks and finally become indistinguishable from those of host neurons. Thus, grafted neurons can integrate with great specificity into neocortical circuits that normally never incorporate new neurons in the adult brain.

Nature 2016; 539: 248

Eitan Israeli

"A lie can travel half way around the world while the truth is putting on its shoes"

Mark Twain (1835-1910), American writer, entrepreneur, publisher and lecturer. Among his novels are *The Adventures of Tom Sawyer* and its sequel *Adventures of Huckleberry Finn*

"No drug, not even alcohol, causes the fundamental ills of society. If we're looking for the source of our troubles, we shouldn't test people for drugs, we should test them for stupidity, ignorance, greed, and love of power"

P.J. O'Rourke (born 1947), American political satirist and journalist

Capsule

Spinal cord regeneration in zebrafish

Unlike humans, zebrafish can regenerate their spinal cord. Mokalled et al. identified a growth factor in zebrafish that helps this process. The protein encoded by ctgfa (*connective tissue growth factor a*) is secreted after injury and encourages glial cells to form a bridge across the spinal lesion. Addition of this protein improved spinal cord repair in injured zebrafish.

Science 2016; 354; 63

Eitan Israeli

"Life is what happens to us while we are making other plans"

Allen Saunders (1899-1986), American writer, journalist and cartoonist

Capsule

Status alters immune function in macaques

Rhesus macaques experience variable levels of stress on the basis of their position in the social hierarchy. To examine how stress affects immune function, Snyder-Mackler et al. manipulated the social status of individual macaques. Social status influenced the immune system at multiple levels, from immune cell numbers to gene expression, and altered signaling pathways in a model of response to infection. Macaques possess a plastic and adaptive immune response wherein social subordination promotes antibacterial responses, whereas high social status promotes antiviral responses.

Science 2016; 354: 1041

Eitan Israeli

Capsule

Exhausting autoimmunity in type 1 diabetes

In the case of autoimmune diseases, such as type 1 diabetes, so-called exhausted T cells may be the answer to stopping disease. Long et al. report that the best responses in type 1 diabetics treated with teplizumab, a monoclonal antibody against CD3, were associated with $CD8^+$ T cells with features of exhausted T cells. These cells recognized a broad spectrum of autoantigens but proliferated less than non-exhausted cells ex vivo. However, they were not terminally exhausted: stimulation with a ligand for the inhibitory receptor TIGIT further down-regulated their activation. Inducing T cell exhaustion may thus represent a potential therapeutic approach in type 1 diabetes.

Sci Immunol 2016; 1: eaai7793

Eitan Israeli

Capsule

Cardiac side effect

Antibodies that block CTLA-4 (cytotoxic T lymphocyte-associated antigen 4) and PD-1 (programmed death 1) allow T cells to launch antitumor immune responses. Although these checkpoint inhibitors improve survival in melanoma patients, inflammation of other tissues is a common side effect. Johnson et al. report that two melanoma patients treated with a combination of the checkpoint inhibitors developed fatal cardiac damage. Biopsies revealed that T cells and macrophages that infiltrated the heart were the same as those found in skeletal muscle and the tumor. Neither patient had cardiac risk factors other than hypertension. Review of a safety database suggests that severe myocarditis from such combination therapy affects less than 1% of patients. The mechanism for this rare toxic effect is not known.

N Engl J Med 2016; 375: 1749

Proc Natl Acad Sci USA 2016; 10.1073/pnas.1603325113

Eitan Israeli

Capsule

Vessel co-option mediates resistance to anti-angiogenic therapy in liver metastases

The efficacy of angiogenesis inhibitors in cancer is limited by resistance mechanisms that are poorly understood. Notably, instead of through the induction of angiogenesis, tumor vascularization can occur through the non-angiogenic mechanism of vessel co-option. Frentzas and co-authors show that vessel co-option is associated with a poor response to the anti-angiogenic agent bevacizumab in patients with colorectal cancer liver metastases. Moreover, the authors found that vessel co-option is also prevalent in human breast cancer liver metastases, a setting where results with anti-angiogenic therapy have been disappointing. In preclinical mechanistic studies, they found that cancer cell motility mediated by the actin-related protein 2/3 complex (Arp2/3) is required for vessel co-option in liver metastases in vivo and that, in this setting, combined inhibition of angiogenesis and vessel co-option is more effective than the inhibition of angiogenesis alone. Vessel co-option is therefore a clinically relevant mechanism of resistance to anti-angiogenic therapy and combined inhibition of angiogenesis and vessel co-option might be a warranted therapeutic strategy.

Nature Med 2016; 22: 1294

Eitan Israel

"If you don't stand for something you will fall for anything"

Anonymous

Capsule

Toward malaria eradication

Even though we know how to prevent malaria, we have failed to eliminate this damaging disease. Bellinger and collaborators designed an easy-to-administer device that provides long-lasting delivery of an anti-malarial drug. A star-shaped, drug-containing material is packaged into a capsule. When swallowed, the capsule dissolves in the stomach and the star unfolds, assuming a shape that cannot pass further down the intestine. The star delivers the anti-malarial drug for weeks, but eventually falls apart and passes harmlessly out of the body.

Sci Transl Med 2016; 8: 365ra157

Eitan Israeli

Capsule

The mechanism of force transmission at bacterial focal adhesion complexes

Various rod-shaped bacteria mysteriously glide on surfaces in the absence of appendages such as flagella or pili. In the deltaproteobacterium *Myxococcus xanthus*, a putative gliding motility machinery (the Agl-Glt complex) localizes to so-called focal adhesion sites (FASs) that form stationary contact points with the underlying surface. Faure et al. show that the Agl-Glt machinery contains an inner membrane motor complex that moves intracellularly along a right-handed helical path; when the machinery becomes stationary at FASs, the motor complex powers a left-handed rotation of the cell around its long axis. At FASs, force transmission requires cyclic interactions between the molecular motor and the adhesion proteins of the outer membrane via a periplasmic interaction platform, which presumably involves contractile activity of motor components and possible interactions with peptidoglycan.

Nature 2016; 539: 530

Eitan Israeli

Capsule

Translocation and dissemination of commensal bacteria in post-stroke infection

Bacterial infection is highly prevalent in patients who have had a stroke. Despite the potential contribution of micro-aspiration in post-stroke pneumonia, Stanley and team found that the majority of microorganisms detected in the patients who developed infections after having a stroke were common commensal bacteria that normally reside in the intestinal tracts. In a mouse model of ischemic stroke, post-stroke infection was only observed in mice that were born and raised in specific pathogen-free facilities; this was not seen in mice that were born and raised in germ-free facilities. Using high-throughput 16S rRNA gene amplicon sequencing and bioinformatics analyses, the authors show that the source of the bacteria forming the microbial community in the lungs of post-stroke mice was indeed the host small intestine. Additionally, stroke-induced gut barrier permeability and dysfunction preceded the dissemination of orally inoculated bacteria to peripheral tissues. This study identifies a novel pathway in which stroke promotes the translocation and dissemination of selective strains of bacteria that originated from the host gut microbiota.

Nature Med 2016; 22: 1277

Eitan Israeli