In La Jolla Institute for Immunology
La Jolla, CA
Miguel Reina -Campos, Ferhat Ay
$1,300,000

Leveraging histonet1ve[1oc9 (on)6.1 1.7 (r)1.8 (a)sr arroir-1.77ton of6 (v c2.8 7(r)1.8 (a)l2.8 (t)lu.9 c9 la)17at1vriye
T cells does not tackle the root problem: the lack of suitable nutrients. Two
rs at the La Jolla Institute for Immunology will attempt to power T cells from
sforming their epigenome into a strategic metabolic asset they can leverage
tions of nutrient starvation. Histones are one of the most abundant cellular
d they harbor large amounts of post -translational modifications. Acetylation
as a particularly prevalent modification among these. An acyl chain can be
y histone deacetylases into acetate and converted to acetyl -CoA, a key versat ile
Histone acetylation levels reflect changes in environmental nutrient availability,
c histone modifications do not always correlate with gene transcription. Thus,
ypothesizes that histones can store large quantities of u seful metabolites,
acting as a cellular nutrient reservoir. Integrating novel functional genetic
stone modification mapping, metabolic tracing, metabolomics, and new tools to
epigenome's architecture, they aim to demonstr ate the potential of
" histone acetylation and to deploy an engineered epigenetic system to
e persistence and function of T cells in immunotherapies.

Montana State University
Bozeman, MT
Dana Rashid, Susan Chapman, Kimberly Coope
$1,000,000

Defining the role of inflammation in vertebrate bone fusion

Inflammation, often viewed as a blight on our health, is known as a response to infection, trauma, or disease. A team of three investigators at Montana State University, Clemson University, and University of California, San Diego hypothesizes that inflammation is a universal driver of vertebrate postnatal bone fusion events. They discovered a critical role of inflammation in normal skeletal maturation that drives vertebral fusion in the avian tail and sacrum, and this fusion is inhibited by anti -inflammator y drugs. To investigate whether inflammation is a widespread bone fusion mechanism, the team will expand their studies to mammals. Kangaroo rat -like rodents called jerboa are ideal for this study as they have extensive axial and peripheral skeletal fusions . The goal is to identify those postnatal bone fusion events in chicken and jerboa that involve inflammation and are vulnerable to anti - inflammatory drugs. The team is also investigating the contribution of necroptosis, an inflammatory type of cell death, to bone fusions in development and disease. For a broader perspective, they will apply an evolutionary lens to examine inflammation as an instigator of evolutionary adaptation. Humans, like other terrestrial vertebrates, undergo extensive postnatal skeleta l fusions that have arisen as evolutionary adaptations. Their data suggests that fusion events could be unintended targets in the clinical application of anti - inflammatory drugs, carrying significant health implications.

Memorial Sloan -Kettering Cancer Center
New York, NY
Chrysothemis Brown, Christina Leslie, Santosha Vardhana
$1,500,000

Recruiting neuronal communication pathways for immune tolerance

The immune system’s ability to avoid attacking the very tissues it is designed to protect is critical to preventing autoimmune diseases. Elucidating the regulatory mechanisms underlying this immune tolerance will open the door to better treatment (o)12Dvmid aTw 0. 71 (y)1.5 (s)2.9 (0. 72e-

Salk Institute for Biological Studies
La Jolla, CA
Terrence Sejnowski, Gerald Pao, Jack Gallant
$1,600,000

Mapping human brain dynamics with generative manifold networks

Three investigators at the Salk Institute, the Okinawa Institute of Science and Technology, and at the University of California at Berkeley, will collaborate to decipher human behavior using a computer model derived from functional magnetic resonance imaging (fMRI). The team aims to generate the same complex human behaviors from their computer model as is created from the recordings. The investigators will use a novel mathematical method called generative manifold networks, which is based on techniques from dynamical systems theory to determine all the cause-and-effect relationships between all the recorded brain areas. These relationships will then be transformed into mathematical objects called manifolds, which will recapitulate the flow of information in the brain. Compared to other methods, this approach aims to capture the essence of biological computing with much less data and fine-tuning, does not require extreme numerical precision, and can tolerate incomplete observations and distorted data without collapsing so long as the relevant information is present. As a proof of concept, the team has recapitulated fly walking and larval zebrafish swimming behaviors from whole-brain optical recordings. High-resolution fMRI recordings will be obtained from humans playing increasingly complex virtual reality video games, and the investigators will then test the model's generated behaviors playing the same games.

Stanford University
Palo Alto, CA
Michael Z. Lin, Brian Kobilka, Vivianne Tawfik
$1,400,000

Developing bioluminescent probes for visualizing GPCR ligand release in the whole body

G protein -coupled receptors (GPCRs) and their ligands play critical roles in governing the intricate physiology of the body. Communicating between organ systems and along the brain -body axis, they maintain homeostasis, respond to threats, and adjust metaboli sm to needs and resources. However, understanding the functions of GPCR ligands in specific tissuhefikfi-5.2 (a)-0.9 li1.6 (e)-a.1 (e)1.6 6(i)11.1 9 bii1.1 (kf-1.7 (s)6.1 (g)4.2 (b)7 d ( )Tj)9.9 (i-5 -0.004 Tc 0 Tw