Targeting Trends 2020 Review

Navigating the Turbulent Waters of the Pandemic

2020 ushered in a new way of life for all of us. The first COVID case was confirmed by the Center for Disease Control (CDC) on January 17. In California, where Advanced Targeting Systems is located, on March 1st, masks were 'strongly recommended' in indoor settings. On March 11, the World Health Organization (WHO) gave pandemic status to COVID-19. By March 19th, a statewide 'Stay-at-Home' order was given.

Around the world, countries and communities were thrust into turmoil trying to get ahead of the virus in a number of different ways. Finding enough protective gear for medical workers dealing with the onslaught of new cases, finding beds and respiratory equipment to take care of hospitalized patients, developing diagnostic tests and vaccines, and enforcing strict guidelines to protect everyone.

For ATS, this meant setting up schedules for employees to work from home, providing masks and hand sanitizer when laboratory work had to be done, and keeping our products and services available to the researchers still in laboratories working on solutions to end the pandemic. Since ATS was working and providing services for development of diagnostics and treatments for COVID-19, we were able to get our employees vaccinated fairly quickly. This was not the case for many of you, and the isolation this caused was devastating.

ATS put many protective measures in place to ensure that there was a clean work environment for our team members. Hand sanitizers and masks were provided for employees and their extended families. We even offered free masks for anyone placing an order.

In this issue:

Life in the Pandemic

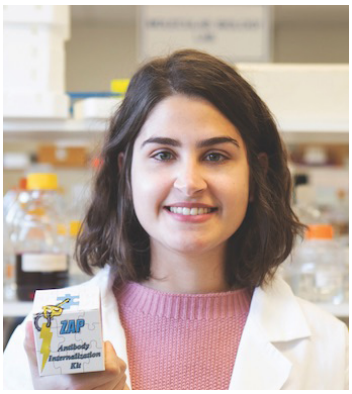
Denise Higgins
President

It was fortunate for ATS that we had just relocated to Carlsbad a month before the pandemic was making an impact in southern California. The new space was set up with an open office design where nobody's desk was closer than six feet to the nearest neighbor. My primary concern was making sure everyone had Personal Protective Equipment (PPE) to give them a level of comfort that they could come in to work and not be exposed to COVID. In the early days there was not much available on the market and what was there was being ravaged by frightened people or, unfortunately, people who wanted to make a profit by reselling at twice the original price. Since I majored in Theatre in college and had good experience in costume making, I thought I'd just investigate the best and safest mask designs and make those for our team and their significant others. It kept me busy outside of business hours and I was also able to give masks to some of the healthcare workers who were also experiencing difficulties in getting the necessary PPE.

We quickly put Zoom meetings into action and were able to hold our weekly meetings and meet with scientists from other institutions without leaving our desks. It allowed us the opportunity to get creative with our presentations so that everyone could see and hear quite well. Whether for business or personal reasons, Zoom allowed us to celebrate occasions with others and have multiple attendees sharing with each other—seeing each other, laughing and enjoying a new kind of social life.

Outdoor activities became the safest way to exercise and socialize. I enjoyed playing golf twice a week, even though we were required to wear a mask and benches and golf ball-washing stations were removed. The upside was that they also removed the rakes from the sand traps and the COVID rules stated you must remove your ball from the sand and place it nearby on the grass. My scores were better than ever!

Looking forward, we've learned some valuable lessons. Wearing a mask, washing your hands frequently and keeping a 6-foot distance from others actually helps you become generally more healthy – fewer colds and other common sicknesses. I'm looking forward to healthy days ahead.



Raschel Bouajram
Product Manager
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With the pandemic came the slowdown of social activities, which gave me more time to read, workout, cook and try new hobbies like making jewelry. It was definitely a time of exploration and appreciation. The pandemic was a good reminder to not take your health and people in your life for granted, and to recognize how fortunate we are to live in a country that can take care of us – even though it was hard to find toilet paper 😝 . I am glad that I was able to stay connected to family and friends who live across the world, since travelling was not an option.

Kristen Hartman
Website &
Database Manager

The pandemic started with extra company when my two college-age children were suddenly home for a few extra months. As the days stretched on, I started reading more than ever. And then we did what many others did and got a new puppy! When we weren't busy taking him for walks, my husband Mason and I also worked on renovating our house.

At the start of 2020, home-life was trying to raise a 3 and 5 year old along with caring for my wife's parents who live with us. By late November, our household was trying to manage the domino effect of one of us contracting the virus and ultimately spreading it to the rest household. Looking back at the challenges, we're seeing how the pandemic helped tip-the-scales regarding certain decisions…and all for the better. My wife and I solidified our decision to homeschool both our kids, where everyone, including my wife, seem to be thriving. Mom and Dad consider themselves lucky and try never to miss a moment of enjoying their grandchildren with tighter hugs, and ATS reminded me that my 'workplace' was more than the place that I work, but a place of support and friendship.

Leonardo Ancheta
Vice-President
Sr Product Manager
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The negatives of the pandemic have been countless. My personal experience was that I struggled with the lack of interaction with friends and family during peak mandates. There have been some bittersweet aspects of the pandemic, like spending more time doing things like gardening and backpacking. Being an essential worker, I still had to come into the lab, but fortunately there was none of the usual traffic on my commute. I even picked up a few new hobbies; at one point I had a sourdough starter and beer fermenting in my kitchen – felt like I was starting a second lab at home. At the end of the day, I feel lucky to have had a dog throughout the pandemic.

Many little life lessons were learned and reaffirmed during the 2020 Pandemic:

- Smile, even when your mask is covering your face, and no one can see.
- Patience. Standing in long masked-up lines for cleaning products, bathroom tissue and vaccine shots.
- Understanding, acceptance without shame that CDC guidelines for many were blurry. Let me do what I need to do to feel safe and you do what you need to do to be comfortable.
- Acceptance that this Pandemic lifestyle may have many on and off sequences regarding masking and staying away from crowds.
- Trusting in others. The few people in my sphere I believe all behaved in a fiduciary manner with regard to my health including written and unwritten agreed upon behaviors and covenants.
- Information. Too much information wasn't the best goal, but reliable sources were.
- Yes, more than a few daily simple life choices changed. Many other life tools were redefined and reaffirmed.

Tom Cobb
Administration Manager

2020 Scientific References

Targeted Toxins

Targeting agent attached to Saporin

IT-01 192-IgG-SAP

Evaluation of the adverse effects of chronic exposure to donepezil (an acetylcholinesterase inhibitor) in adult zebrafish by behavioral and biochemical assessments. Audira G et al. Biomolecules 10(9):1340, 2020.

Objective: The authors use zebrafish to conduct a deeper analysis of the potential adverse effects of donepezil (DPZ) on the short-term memory and behaviors of normal zebrafish by performing multiple behavioral and biochemical assays.

Summary: Chronic waterborne exposure to DPZ can severely induce adverse effects on normal zebrafish in a dose-dependent manner.

See: Cutuli D et al. Alzheimers Res Ther 5(5):50, 2013.

Long-term potentiation in the hippocampal CA3 to CA1 synapses may be induced in vivo by activation of septal cholinergic inputs. Dobryakova YV et al. Int J Neurosci 23:1-7, 2020.

Objective: To clarify the role of septal input in the development of long-term potentiation (LTP) in this synapse.

Summary: Elimination of septal cholinergic neurons by 192-IgG-SAP abolished LTP development in both experimental series. This suppression of LTP in animals with a cholinergic deficit was not due to loss of hippocampal neurons.

Dose: Rats received intraseptal injections of 192-IgG-SAP (1.5 µg).

Cholinergic signaling dynamics and cognitive control of attention. Parikh V et al. Shoaib M., Wallace T (Ed.): Behavioral Pharmacology of the Cholinergic System. Current Topics in Behavioral Neurosciences. 45:71-87, 2020. Springer, Cham

Summary: A plethora of studies conducted in rodents demonstrated that selective lesions of BF cholinergic neurons and their cortical inputs produced by the immunotoxin 192-IgG-SAP impair performance in various tasks of attention.

Acetylcholine and spontaneous recognition memory in rodents and primates. Easton A et al. Curr Top Behav Neurosci 45:29-45, 2020.

Summary: Review of lesioning designed to specifically target cells that express acetylcholine as a transmitter.

Measuring attention in rats with a visual signal detection task: Signal intensity vs. signal duration. Holloway Z et al. Pharmacol Biochem Behav 199:173069, 2020.

Summary: Drug-induced effects have been used to demonstrate the construct validity of operant attention tasks, as well as to assess the pharmacological systems that underlie cognitive processes, such as attention, short-term memory and reaction time, either by interrupting or enhancing performance.

See: McGaughy J et al. Behav Neurosci 112(6):1519-1525, 1998.

Extracellular levels of the sleep homeostasis mediator, adenosine, are regulated by glutamatergic neurons during wakefulness and sleep. Sun MJ et al. Purinergic Signal 16(4):475-476, 2020.

Summary: Blanco-Centurion et al. investigated the role of cholinergic neurons in the BF by administering 192–IgG–SAP to lesion them, but surprisingly the results indicated that adenosine from cholinergic neurons in BF are not essential to sleep induction.

See: Blanco-Centurion C et al. J Neurosci 26(31):8092-8100, 2006.

Intracerebroventricular administration of 192IgG-saporin alters the state of microglia in the neocortex. Volobueva MN et al. Neurochem J 14(1):37-42, 2020.

Objective: The effect of (icv) immunotoxin administration on the state of microglia in tissues adjacent to the ventricle (striatum and parietal cortex) and remotely located but receiving innervation from the medial septal region and diagonal band of Broca (entorhinal cortex and olfactory bulbs).

Summary: 1.5 months after the administration of immunotoxin, microglia are activated only in the neocortical areas, not in the striatum or olfactory bulbs.

Dose: Injected bilaterally at a dose of 4 µg in each ventricle.

IT-02 OX7-SAP, special order

Reversal of object recognition memory deficit in perirhinal cortex-lesioned rats and primates and in rodent models of aging and alzheimer's diseases. Masmudi-Martín M et al. Neuroscience 448:287-298, 2020.

Objective: To determine if Object Recognition Memory (ORM) can be restored.

Summary: Memory-deficient rats were generated by induction of lesions to the perirhinal cortex (PRh) through an injection of OX7-SAP. Expression of regulator of G-protein signaling 14 of 414 amino acids (RGS14414) restored ORM in memory-deficient PRh-lesioned rats and nonhuman primates. This treatment was sufficient for full recovery of ORM in rodent models of aging and Alzheimer's disease.

Dose: Rats were injected with OX7-SAP (0.9 mg in 1ml) in the PRh of the brain

IT-03 Anti-DBH-SAP

Noradrenaline signaling in the LPBN mediates amylin's and salmon calcitonin's hypophagic effect in male rats. Boccia L et al. FASEB J 34(11):15448-15461, 2020.

Objective: To assess the phenotype of amylin activated LPBN (lateral parabrachial nucleus) neurons, especially to confirm the CGRPergic phenotype and to uncover the specific role of NA (noradrenaline) signaling from the AP to the LPBN.

Summary: The present study confirmed the central role of the LPBN in propagating amylin's and sCT's hypophagic action, and particularly the importance of AP → LPBN NA signaling in the mediation of this process, through the activation of LPBN (CGRP and non-CGRP) neurons.

Dose: The neuronal pathways used to process the physiological response to amylin were investigated using 50-ng injections of Anti-DBH-SAP (Cat. #IT-03) into the area postrema (AP) or 25 ng into the lateral parabrachial nucleus (Potes et al., 2010).

2020 Scientific References

Corticolimbic stress regulatory circuits, hypothalamo–pituitary–adrenocortical adaptation, and resilience. Herman JP Chen A (Ed.): Stress Resilience 291-309, 2020. Academic Press

Summary: Review. Immunolesion of paraventricular nucleus (PVN)-projecting norepinephrine (NE) neurons with Anti-DBH-SAP attenuates acute stress reactivity (interestingly, to restraint), but it does not inhibit somatic or HPA axis responses to stress in any simple way (Flak et al., 2014). PVN-projecting NE neurons appear to be responsible for acute responses to systemic stressors, but they do not appear to be important in mediating effects of chronic stress (Ritter et al., 2003).

Dose: Flak et al. injected 8.82 ng of Anti-DBH-SAP into the PVN. Ritter et al. injected 42 ng into the PVN.

An age- and sex-dependent role of catecholaminergic neurons in the control of breathing and hypoxic chemoreflex during postnatal development. Patrone LGA et al. Brain Res 1726:146508, 2020.

Objective: To discover the role of brainstem catecholaminergic (CA) neurons in the hypoxic ventilatory response (HVR).

Summary: Brainstem CA neurons modulate the HVR during the postnatal phase, and possibly thermoregulation during hypoxia.

Dose: Evaluation of brainstem CA neurons in the HVR during postnatal development in male and female rats through specific cell depletion with Anti-DBH-SAP (420 ng/nL) injected in the fourth ventricle.

Loss of diffuse noxious inhibitory control after traumatic brain injury in rats: A chronic issue. Irvine KA et al. Exp Neurol 333:113428, 2020.

Objective: To confirm hypothesis that dysfunctional descending noradrenergic and serotonergic pain control circuits may contribute to the loss of diffuse noxious inhibitory control (DNIC), a critical endogenous pain control mechanism, weeks to months after traumatic brain injury (TBI).

Summary: Results suggest that TBI causes maladaptation of descending nociceptive signaling mechanisms and changes in the function of both adrenergic and serotonergic circuits. Such changes could predispose those with TBI to chronic pain.

Dose: Anti-DBH-SAP (5 µg/5 µl) was injected in the left ventricle. Lesion of the LC resulted in failure of DNIC, an effect that mimics what is observed behaviorally after chronic TBI.

Adrenergic supersensitivity and impaired neural control of cardiac electrophysiology following regional cardiac sympathetic nerve loss. Tapa S et al. Sci Rep 10:18801, 2020.

Summary: The authors present a novel mouse model of regional cardiac sympathetic hypo-innervation utilizing Anti-DBH-SAP.

Dose: Either 5µL of 40 ng/µL Anti-DBH-SAP or Mouse IgG-SAP (control) was applied three times directly to the exposed apical/anterior surface of the heart.

Integration of peripheral and central systems in control of ingestive and reproductive behavior. Schneider J Oxford Research Encyclopedia of Neuroscience , 2020. Oxford University Press

Summary: Highly glucose-sensitive cells in the ventrolateral medulla send catecholaminergic projections to the PVH. These projections can be selectively destroyed by Anti-DBH-SAP “DSAP” experiments show that catecholaminergic projections from glucose-sensitive cells in the ventrolateral medulla are necessary for all responses to glucoprivation, including increases in epinephrine secretion, glucocorticoid secretion, sex behavior, and food intake.

See: Ritter S Physiol Behav 208:112568, 2019.

Depletion of C1 neurons attenuates the salt-induced hypertension in unanesthetized rats. Ribeiro N et al. Brain Res 1748:147107, 2020.

Objective: To determine if the ablation of C1 neurons mitigates high blood pressure induced by high-salt intake.

Summary: Data show that hypertension induced by high-salt intake is dependent on C1 neurons.

Dose: Bilateral injections of 2.4 ng/100 nl of Anti-DBH-SAP. The total number of TH+ neurons in the AS region was reduced by 37 ± 13% in the anti-DBH-SAP group when compared to control.

Neuroendocrine and behavioral consequences of hyperglycemia in cancer. Vasquez JH et al. Endocrinology 161(5):bqaa047, 2020.

Summary: Ablation of norepinephrine containing projections to the arcuate (via Anti-DBH-SAP injections) alters AgRP and neuropeptide (NPY) concentrations, leading to impairments in hypoglycemic (glucoprivic) or ghrelin-induced feeding.

Dose: Anti-DBH-SAP (bilateral 42-ng intracranial injections) was used in rats to investigate the role of hindbrain catecholamine afferents in increased ARC NPY and AgRP gene expression.

See: Fraley GS et al. Endocrinology 144(1):75-83, 2003.

2020 Scientific References

IT-06, IT-33 Mac-1-SAP

Inflammatory macrophages facilitate mechanical stress-induced osteogenesis. Zhang F et al. Aging (Albany NY) 12(4):3617-3625, 2020.

Summary: In a mouse model of distraction osteogenesis (DO), there was significant increase in macrophages in the regeneration area. This suggests that targeting inflammatory macrophages may help to improve clinical bone repair.

Dose: For saporin-mediated depletion of macrophages, DO-surgery-treated mice received an intraventricular (iv) injection of either Mac-1-SAP or Rat IgG-SAP (20µg) once every 3 days.

Spinal microglia-neuron interactions in chronic pain. Ho et al. J Leukoc Biol 108:1575-1592, 2020.

Summary: Spinal microglial activation is initiated shortly and persisted for more than 3 mo after partial sciatic nerve ligation. Intrathecal injection of Mac1-SAP, a saporin-conjugated anti-CD11b antibody to deplete microglia, abolished cold and mechanical allodynia for 2–12 wk after injury,92 supporting the role of activated microglia for chronic pain maintenance.

See: Echeverry S et al. Pain 158:1792-1801, 2017.

IT-11 SSP-SAP

Central circuit mechanisms of itch. Chen XJ et al. Nat Commun 11:3052, 2020.

Summary: The authors summarize the progress in elucidating the neural circuit mechanism of itch at spinal and supraspinal levels.

A role for neurokinin 1 receptor expressing neurons in the paratrigeminal nucleus in bradykinin-evoked cough in guinea-pigs. Driessen AK et al. J Physiol 598(11):2257-2275, 2020.

Objective: This study aimed to assess the involvement of paratrigeminal neurokinin 1 receptor neurons in the regulation of cough, breathing and airway defensive responses.

Dose: Targeted toxin lesions across three sites of the paratrigeminal nucleus (200nl per injection site).

IT-14 CTB-SAP

Differential mechanisms are required for phrenic long-term facilitation over the course of motor neuron loss following CTB-SAP intrapleural injections. Borkowski LF et al. Exp Neurol 334:113460, 2020.

Objective: To understand the mechanism responsible for this difference in magnitude of phrenic long-term facilitation (pLTF)

Summary: pLTF in 7d CTB-SAP treated rats is elicited primarily through TrkB and PI3K/Akt-dependent mechanisms, whereas BDNF and MEK/ERK-dependent mechanisms induce pLTF in 28d CTB-SAP treated rats.

Dose: Rats received bilateral intrapleural injections of CTB-SAP; 25 µg dissolved in PBS.

Local riluzole release from a thermosensitive hydrogel rescues injured motoneurons through nerve root stumps in a brachial plexus injury rat model. Fang J et al. Neurochem Res 45(11):2800-2813, 2020.

Summary: The authors refer to a review by Gulino describing two rodent models of motoneuron degeneration were induced by neurotoxics including volkensin and cholera toxin-B saporin, which are able to destroy motoneurons through retrograde transportation.

See: Gulino R Neural Plast 2016:2769735, 2016.

Exercise promotes recovery after motoneuron injury via hormonal mechanisms. Chew C et al. Neural Regen Res 15(8):1373-1376, 2020.

Objective: To describe how exercise is neuroprotective for motoneurons, accelerating axon regeneration following axotomy and attenuating dendritic atrophy following the death of neighboring motoneurons.

Summary: Exercise offers a simple, low barrier-to-entry behavioral intervention which is neuroprotective and pro-regenerative following neural injury.

Dose: Motoneurons innervating the left vastus medialis muscle were selectively killed by intramuscular injection of CTB-SAP (2 µL, 0.1%).

Respiratory pathology in the Optn-/- mouse model of Amyotrophic Lateral Sclerosis. McCall AL et al. Respir Physiol Neurobiol 282:103525, 2020.

Summary: Tongue muscle weakness results in dysarthria and dysphagia leading to recurrent aspiration, choking, and aggravation of respiratory disease.

See: Lind LA et al. Neuroscience 390:303-316, 2018.

IT-23 Anti-SERT-SAP

Using loss- and gain-of-function approaches to target amygdala-projecting serotonergic neurons in the dorsal raphe nucleus that enhance anxiety-related and conditioned fear behaviors. Bernabe CS et al. J Psychopharmacol 34(4):400-411, 2020.

Objective: To investigate the role of amygdala-projecting 5-HT neurons in the DR in innate anxiety and conditioned fear behaviors.

Dose: Each rat received two bilateral microinjections per site (100 nL each, 1 µM in artificial cerebrospinal fluid) of either Anti-SERT-SAP or the control Mouse IgG-SAP.

IT-40 Bombesin-SAP

Spinal GRPR and NPRA contribute to chronic itch in a murine model of allergic contact dermatitis. Liu X et al. J Invest Dermatol 140(9):1856-1866.e7, 2020.

Objective: The authors investigated the peripheral and spinal mechanisms responsible for prolonged itch in a mouse model of allergic contact dermatitis (ACD) induced by squaric acid dibutylester (SADBE).

Summary: Targeting gastrin-releasing peptide receptor (GRPR) and natriuretic peptide receptor A (NPRA) may provide effective treatments for ACD associated chronic pruritus.

Dose: A single dose of Bombesin-SAP (400 ng) and Blank-SAP (400 ng) or two doses of Nppb-SAP (BNP-SAP; 650 ng) and Blank-SAP (650 ng) were administered via intrathecal injection.

2020 Scientific References

Exploration of sensory and spinal neurons expressing gastrin-releasing peptide in itch and pain related behaviors. Barry DM et al. Nat Commun 11(1):1397, 2020.

Objective: To determine the role of GRP in sensory neurons.

Summary: GRP is a neuropeptide in sensory neurons for nonhistaminergic itch, and GRP sensory neurons are dedicated to itch transmission.

Dose: Bombesin-SAP (200 ng/5 µL, i.t.) was injected 2 weeks prior to optical stimulation.

More than scratching the surface: recent progress in brain mechanisms underlying itch and scratch. Liu X et al. Neurosci Bull 36(1):85-88, 2020.

Summary: The discovery of descending neural circuitry to drive the itch-scratching cycle may provide potential therapeutic targets in the central nervous system for the management of chronic itch.

Dose: To ablate the spinal GRPR+ neurons, mice were intrathecally injected with Bombesin-SAP or Blank-SAP (400 ng/5 mL).

See: Gao ZR et al. Neuron 101(1):45-59.e9, 2019.

GRP receptor and AMPA receptor cooperatively regulate itch-responsive neurons in the spinal dorsal horn. Kiguchi N et al. Neuropharm 170:108025, 2020.

Objective: To investigate the mechanisms for the activation of itch-responsive GRPR+ neurons in the spinal dorsal horn (SDH).

Summary: These findings demonstrate that GRP and glutamate cooperatively regulate GRPR+ AMPAR+ neurons in SDH, mediating itch sensation. GRP–GRPR and the glutamate–AMPAR system may play pivotal roles in the spinal transmission of itch in rodents and nonhuman primates.

Dose: Bombesin-SAP and Blank-SAP were administered i.t. (5 µg/5 µl).

IT-42 Anti-ChAT-SAP

An acetylcholine-dopamine interaction in the nucleus accumbens and its involvement in ethanol's dopamine-releasing effect. Loftén A et al. Addict Biol 26(3):e12959, 2021.

Summary: Basal extracellular levels of dopamine within the nucleus accumbens are not sustained by muscarinic acetylcholine, whereas accumbal Cholinergic interneurons-ACh are involved in mediating ethanol-induced dopamine release.

Dose: Anti-ChAT-SAP or Rabbit IgG-SAP were infused at a flow rate of 0.05 µl/min for 10 min giving a total volume of 0.5 µl.

IT-47 Leptin-SAP

Loss of leptin receptor-expressing cells in the hindbrain decreases forebrain leptin sensitivity. Harris RBS Am J Physiol Endocrinol Metab 318(5):E806-E816, 2020.

Objective: This study tested whether loss of hindbrain leptin receptor signaling changed sensitivity to forebrain leptin.

Summary: Loss of VMH (ventromedial nucleus of hippocampus) leptin receptor-expressing cells prevents weight loss. The integrated response between the hindbrain and forebrain is heavily dependent upon leptin activity in the VMH.

Dose: To test forebrain leptin sensitivity Leptin-SAP and Blank-SAP rats received third ventricle injections of 0, 0.05, 0.1, 0.25 or 0.5 µg leptin.

IT-69 Nppb-SAP

Spinal GRPR and NPRA Contribute to Chronic Itch in a Murine Model of Allergic Contact Dermatitis. Liu X et al. J Invest Dermatol 140(9):1856-1866.e7, 2020.

see IT-40 Bombesin-SAP for summary

Intervening B-Type Natriuretic Peptide Signaling for Controlling Chronic Itch. Meng J et al. Brit J Pharmacol 177(5):1025-1040, 2020.

Objective: Review of recent findings used to examine the role of B-type natriuretic peptide (BNP) in itch transduction and the modulation of other pururitic proteins.

Summary: Mice treated with Nppb-SAP ablated 70% of the BNP receptor-positive neurons in the spinal cord.

Molecular Genetics of Kappa Opioids in Pain and Itch Sensations. Tseng PY et al. Handb Exp Pharmacol, 2020.

Summary: The authors review the functions of the kappa opioid receptor (KOR) and its endogenous agonists dynorphins in modulating itch and pain. Nppb-SAP ablation of neurons expressing the Natriuretic olypeptide B receptor greatly reduced itch responses evoked by histamine or by intrathecal administration of Nppb, suggesting these neurons transmit itch signals from Nppb primary afferents.

See: Mishra SK et al. Science 340(6135):968-971, 2013.

Reviews

Identification of multiple targets in the fight against Alzheimer's disease. Giannoni P et al. Front Aging Neurosci 12:169, 2020.

A collection of 20 articles that depict a broad representation of the most impactful advances in Alzheimer's disease (AD) comprehension and therapeutic openings.

Saporin from Saponaria officinalis as a tool for experimental research, modeling, and therapy in neuroscience. Bolshakov AP et al. Toxins (Basel) 12(9):546, 2020.

A review of studies where saporin-based conjugates were used to analyze cell mechanisms of sleep, general anesthesia, epilepsy, pain, and development of Parkinson's and Alzheimer's diseases.

2020 Scientific References

Custom Conjugates

Superior mouse eosinophil depletion in vivo targeting transgenic Siglec-8 instead of endogenous Siglec-F: Mechanisms and pitfalls. Knuplez E et al. J Leukoc Biol 108:43-58, 2020.

Objective: To determine if targeting Siglec-8 with mouse IgG1 antibodies, rather than with rat IgG antibodies, in mice transgenic for Siglec-8, will prove to be a more effective strategy for eliminating mouse eosinophils in vivo.

Summary: This study is the first to describe a novel mouse strain of Siglec-8+F− eosinophils—a useful tool for studying human Siglec biology in preclinical models.

Dose: Siglec-8+F− mouse eosinophils were pretreated with 10 µg/mL saporin-conjugated isotype controls (mouse IgG1 or rat IgG2), anti-Siglec-8 (2C4) or anti-Siglec-F (9C7) antibodies for 24 h.

Labeling neuronal proteins with quantum dots for single-molecule imaging. Thal LB et al. Methods Mol Biol 2135:169-177, 2020.

Objective: The authors describe how nanometer-sized fluorescent semiconductors called quantum dots (QD) can be used to label neuronal proteins in a single QD imaging format.

Dose: Secondary antibody-conjugated QDs target membrane proteins pre-treated with SERT Mouse Monoclonal.

Cholinergic basal forebrain degeneration due to obstructive sleep apnoea increases Alzheimer's pathology in mice. Qian L et al. bioRxiv 2020.03.12.989848, 2020.

Dose: bilateral injections of urotensin II-saporin (UII-SAP; 0.07 µg/µL per site – unless stated otherwise; generous gift from Advanced Targeting Systems)

Saporin

Characterization of fever and sickness behavior regulated by cytokines during infection. Li W et al. Behaviour 157:855-878, 2020.

Summary: This study reviews the characterization of fever and sickness behavior regulated by cytokines during infection.

Dose: IL-1β-saporin or unconjugated Saporin as control (icv or ip, 1.75 µg) eliminated IL-1R1-expressing cells in the hippocampus and indicated these neurons mediate the function of peripheral IL-1β induced hypophagia.

Intracellular delivery methods using biofunctional peptide-modified extracellular vesicles. Nakase I Extracell Vesicles Circ Nucleic Acids 1:44, 2020. American Society for Exosomes and Microvesicles 2020 Annual Meeting

Summary: Extracellular vesicles (exosomes, EVs) with encapsulation of biofunctional molecules (e.g., enzymes and genes) are highly expected to be next-generation therapeutic carriers because of their pharmaceutical advantages. Saporin-artificially encapsulated EVs with modification of the (sC18)2 peptides showed glycosaminoglycan-dependent cell-killing activity. Our experimental techniques and findings are considered to contribute to the development for EV-based intracellular delivery system via macropinocytosis.

Control Conjugates

IT-21 Blank-SAP

Cholinergic basal forebrain degeneration due to obstructive sleep apnoea increases Alzheimer's pathology in mice. Qian L et al. bioRxiv 2020.03.12.989848, 2020.

See Custom Conjugates

GRP receptor and AMPA receptor cooperatively regulate itch-responsive neurons in the spinal dorsal horn. Kiguchi N et al. Neuropharmacology 170:108025, 2020.

See IT-40 Bombesin-SAP

Loss of leptin receptor-expressing cells in the hindbrain decreases forebrain leptin sensitivity. Harris RBS Am J Physiol Endocrinol Metab 318(5):E806-E816, 2020.

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see IT-40 Bombesin-SAP

IT-17 Rat IgG-SAP

Inflammatory macrophages facilitate mechanical stress-induced osteogenesis. Zhang F et al. Aging (Albany NY) 12(4):3617-3625, 2020.

See IT-06 Mac-1-SAP

IT-18 Mouse IgG-SAP

Adrenergic supersensitivity and impaired neural control of cardiac electrophysiology following regional cardiac sympathetic nerve loss. Tapa S et al. Sci Rep 10:18801, 2020.

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See IT-23 Anti-SERT-SAP

IT-35 Rabbit IgG-SAP

An acetylcholine-dopamine interaction in the nucleus accumbens and its involvement in ethanol's dopamine-releasing effect. Loftén A et al. Addict Biol 26(3):e12959, 2020.

See IT-42 Anti-ChAT-SAP

2020 Scientific References

ZAP Secondary Conjugates

ZAP conjugates are non-targeted saporin conjugates that "piggyback" on to your primary targeting agent

IT-27 Streptavidin-ZAP

Pseudomonas Exotoxin A Based Toxins Targeting Epidermal Growth Factor Receptor for the Treatment of Prostate Cancer. Fischer A et al. Toxins (Basel) 12(12):753, 2020.

Summary: Refers to chimeric murine-human mAb cetuximab bound to Streptavidin-ZAP.

See: Yip WL et al. Mol Pharm 4(2):241-251, 2007.

ALPPL2 is a highly specific and targetable tumor cell surface antigen. Su Y et al. Cancer Res 80(20):4552-4564, 2020.

Objective: To evaluate therapeutic potential of ALPPL2 targeting.

Summary: Exquisite tissue specificity and broad tumor type coverage suggest that ALPPL2 could be an excellent cell surface target for therapeutic development against mesothelioma.

Dose: Biotinylated M25 IgG1 and Streptavidin-ZAP were mixed at a molar ratio of 1:1.

IT-04 Mab-ZAP

Cellular uptake of vitamin B12: Role and fate of TCblR/CD320, the transcobalamin receptor. Gick GG et al. Exp Cell Res 396(1):112256, 2020.

Summary: The increased and sustained expression of TCblR in proliferating cells has been used to target toxins preferentially to cancer cells and can be potentially used for targeted delivery of other anti-cancer drugs. In 2010 the authors published a paper which evaluated the potential of using immunotoxins to eliminate cancer cells expressing TCblR the authors performed a series of in vitro experiments using their monoclonal antibody plus Mab-ZAP in varying concentrations. The results indicated that this is a viable therapeutic model that causes minimal peripheral damage.

The EphA2 and cancer connection: potential for immune-based interventions. London M et al. Mol Biol Rep 47(10):8037-8048, 2020.

Summary: The authors review the most current mAb-based therapies against EphA2-expressing cancers currently in pre-clinical and/or clinical stages. They reference Sakamoto et al. who performed in vitro testing of two different EphA2 mAbs mixed with Mab-ZAP to discover their therapeutic potential against melanoma.

Selected Antibodies

AB-N27AP Anti-Angiotensin II receptor

Chronic treatment with apelin, losartan and their combination reduces myocardial infarct size and improves cardiac mechanical function. Abbasloo et al. Clin Exp Pharmacol Physiol 47:393-402, 2020.

1:10000

Characterization of the renin-angiotensin system in aged cavernosal tissue and its role in penile fibrosis. Bragina ME et al. J Sex Med 17:2129–2140, 2020.

Immunohistochemistry (1:800)

Activation of the renin-angiotensin system in high fructose-induced metabolic syndrome. Kim M et al. Korean J Physiol Pharmacol 24(4):319-328, 2020.

Immunohistochemistry

AB-N38 Anti-Melanopsin

nGnG amacrine cells and Brn3b-negative M1 ipRGCs are specifically labeled in the ChAT-ChR2-EYFP mouse. Cui LJ et al. Invest Ophthalmol Vis Sci 61(2):14, 2020.

Immunostaining 1:10000

Examination of zinc in the circadian system. Moshirpour M et al. Neuroscience 432:15-29, 2020.

Retinal immunohistochemistry (1:5000)

AB-T044 Anti-Conj Trans-4-Hydroxy-L-Proline

Proline hydroxylation primes protein kinases for autophosphorylation and activation. Lee SB et al. Mol Cell 79(3):376-389.e8, 2020.

Western blot

Obesity shapes metabolism in the tumor microenvironment to suppress anti-tumor immunity. Ringel AE et al. Cell 183(7):1848-1866.e26, 2020.

Immunoprecipitation

Vitamin C decreases VEGF expression levels via hypoxia-inducible factor-1α dependent and independent pathways in lens epithelial cells. Zhao L et al. Mol Med Rep 22(1):436-444, 2020.

Western blot (1:500)

AB-T125 Anti-Conjugated NO-L-Cysteine

A DNA-based fluorescent probe maps NOS3 activity with subcellular spatial resolution. Jani MS et al. Nat Chem Biol 16:660–666, 2020.

Immunofluorescence

BT-17AP Biotin-labeled Anti-Saporin

Quantum dot conjugated saporin activates microglia and induces selective substantia nigra degeneration. Landrigan J et al. NeuroToxicology 76:153-161, 2020.

Top 20 Targeting Tools of 2020

Top 5 Targeted Toxins

#1. CTB-SAP (Cat. #IT-14)
targets cells expressing GM1 receptor

#2. Anti-DBH-SAP (Cat. #IT-03)
targets cells expressing rat dopamine beta-hydroxylase

#3. IB4-SAP (Cat. #IT-10)
targets cells expressing alpha-D-galactopyranoside residues

#4. mu p75-SAP (Cat. #IT-16)
targets cells expressing mouse p75NTR

#5. ME20.4-SAP (Cat. #IT-15)
targets cells expressing multiple mammalian species of p75NTR

Top 5 ZAP Products

#1. Streptavidin-ZAP (Cat. #IT-27)
Uses your biotinylated material

#2. Fab-ZAP human (Cat. #IT-51)
Uses your primary human monoclonal antibody

#3. Fab-ZAP mouse (Cat. #IT-48)
Uses your primary mouse monoclonal antibody

#4. Fab-ZAP rat (Cat. #IT-55)
Uses your primary rat monoclonal IgG antibody

#5. FabFc-ZAP human (Cat. #IT-65)
Uses your primary human monoclonal IgG antibody

Top 5 in Number of Publications

#1. 192-IgG-SAP (Cat. #IT-01)
targets cells expressing rat p75NTR

#2. Anti-DBH-SAP (Cat. #IT-03)
targets cells expressing rat dopamine beta-hydroxylase

#3. CTB-SAP (Cat. #IT-14)
targets cells expressing GM1 receptor

#4. SSP-SAP (Cat. #IT-11)
targets cells expressing substance P receptor (NK-1)

#5. Bombesin-SAP (Cat. #IT-40)
targets cells expressing express gastrin releasing peptide (GRP) receptor

Top 5 Antibodies

#1. Melanopsin Rabbit Polyclonal, affinity-purified (Cat. #AB-N39)

#2. Anti-Conjugated Trans-4-Hydroxy-L-Proline (Cat. #AB-T044)

#3. Angiotensin II receptor (AT-2R) Rabbit Polyclonal, affinity-purified (Cat. #AB-N28AP)

#4. NGFr (mu p75) Rabbit Polyclonal, affinity-purified (Cat. #AB-N01AP)

#5. Angiotensin II receptor (AT-1R) Rabbit Polyclonal, affinity-purified (Cat. #AB-N27AP)