

Biogenic amines generated in the rumen that could lead to inflammation include histamine, tyramine, and ethanolamine. Histamine that is absorbed from the rumen or produced endogenously in tissues during inflammation plays a key role in the development of laminitis. Ethanolamine derived from bacterial phospholipids has the potential to enhance growth and virulence of certain gut pathogens. In conclusion, ruminal microbes and their products generate many complex interactions with the host immune system, and dysbiosis has the potential to induce systemic inflammation. Although inflammation is a protective reaction, the persistence of inflammatory mediators could have negative consequences for the host.

**Key Words:** ruminal microbes, dysbiosis, inflammation

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### 0187 Usefulness (or not) of inflammatory biomarkers:

**The good, the bad, and ugly.** C. Chase\*, *South Dakota State University, Brookings.*

The innate immune system has the job of sensing the host's environment—looking for infections and tissue damage. It then does its second job, which is to recruit in the “right” cells to handle the problem. There is ample evidence that both physical and psychological distress can induce innate immune system pro- and anti-inflammatory cytokines that can cause immune dysfunction in animals, leading to an increased incidence of infectious disease. In livestock, there are several factors that will compromise immune function. There is the stress of transportation, dehydration, feed change (with the resulting negative energy balance), acidosis, and associated microbial changes in the gut. Overstimulation of the innate immune system can result in a pro-inflammatory cytokine storm, which will increase tissue damage. Both pro-inflammatory cytokines [such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-1, and interleukin-6] and anti-inflammatory cytokines (such as interleukin 10, transforming growth factor  $\beta$  and interleukin 1 receptor antagonist) can be elevated in the serum of animals experiencing a cytokine storm. These in addition to acute phase proteins are often monitored to “measure inflammation”. An overview of “inflammation” and an experimental approach in cattle to study these local interactions will be discussed along with the proof of concept immunological measurements.

**Key Words:** innate immunity, inflammation, pro-inflammatory, anti-inflammatory

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### 0188 Nutritional and management considerations in beef cattle experiencing stress-induced inflammation.

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When transported to feedlots, beef cattle are exposed to several stressors within a short period of time that directly impact their performance and welfare. The main stressors associated with this “feedlot transfer phase” (FTP)—weaning, road transport, and feedlot entry—increased ( $P < 0.05$ ) plasma concentrations

of cortisol, pro-inflammatory cytokines, and acute-phase proteins (APP), while the magnitude of this response was negatively correlated ( $r = -0.50$ ,  $P < 0.01$ ) with feedlot receiving ADG and DMI. Further, feed and water deprivation elicited ( $P < 0.01$ ) an APP response and reduced ( $P < 0.03$ ) receiving performance similarly as in cattle transported for long distances. Hence, strategies to alleviate the APP response elicited during the FTP were evaluated: (1) Steers were assigned to continuous road transport for 1300 km (TRANS), or road transport for 1300 km with rest stops every 430 km (STOP). During feedlot receiving, ADG and G:F were similar ( $P > 0.68$ ) between TRANS and STOP. Plasma concentrations of APP were greater ( $P \leq 0.04$ ) in TRANS compared with STOP on d 1 of receiving. (2) Steers transported for 1300 km received (SUP) or not (CON) Ca soaps of soybean oil during a 28-d preconditioning. Upon transport, plasma TNF- $\alpha$  increased for CON but decreased for SUP steers ( $P < 0.01$ ). Steers assigned to SUP had greater ( $P = 0.02$ ) ADG compared with CON steers during the receiving phase. Upon slaughter, carcass yield grade and marbling were greater ( $P < 0.05$ ) for SUP compared with CON. A subsequent trial evaluated the inclusion of camelina meal in similar research design. During feedlot receiving, SUP steers had reduced ( $P < 0.01$ ) plasma APP concentrations and tended ( $P = 0.10$ ) to have greater G:F compared with CON. (3) Steers were transported for 1300 km and administered flunixin meglumine (1.1 mg/kg BW) at truck loading and unloading, or meloxicam (1 mg/kg of BW) at loading and during the initial 7 d of feedlot receiving. Both anti-inflammatory drugs reduced ( $P < 0.05$ ) the APP response elicited during the FTP compared with non-treated cohorts, but only meloxicam increased ( $P < 0.04$ ) receiving ADG and G:F. In summary, inclusion of rest-stops during transport, preconditioning PUFA supplementation, and use of anti-inflammatory drugs are alternatives to alleviate the APP response elicited during the FTP, whereas PUFA and meloxicam administration enhanced feedlot performance of feeder cattle.

**Key Words:** beef cattle, inflammation, management, nutrition

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## CELL BIOLOGY SYMPOSIUM: MEMBRANE TRAFFICKING AND SIGNAL TRANSDUCTION

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### 0189 Introduction: What is the relevance of this topic?

J. L. Klotz\*, *USDA-ARS, Forage-Animal Production Research Unit, Lexington, KY.*

Knowledge of membrane dynamics and receptor-ligand related responses are critical to a complete understanding of many of the tissue-level and whole animal level observations made in physiologic, pharmaceutical and toxicological research. The outcome of this basic research can have significant implications in animal agriculture in terms of impact

of disease states, toxin exposure, and use of pharmaceutical and natural products on various aspects of animal production. Can studies that further the understanding of the membrane trafficking and cell signaling relationship be applied to solve problems relevant to livestock production? How do disease states alter the trafficking-signaling interconnection? To answer these questions, the objective of this symposium is to address protein and lipid aspects of transport within a membrane, how functions may change as a result of a pathological state, and how this basic science can be used to further the needs of livestock at the production level.

**Key Words:** cell signaling, livestock production, membrane trafficking

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#### **0190 SNAREs in exocytosis and membrane trafficking.**

S. W. Whiteheart\*, *University of Kentucky, Lexington.*

In 1993, Rothman and colleagues sought to explain the specificity of membrane trafficking between cellular compartments by proposing the SNARE hypothesis. Since that time, we have gained significant insights into the conserved mechanisms that control membrane fusion in all eukaryotes. Integral membrane proteins called SNAREs (Soluble NSF Attachment protein Receptors) mediate the membrane fusion that is required to move cargo from one cellular compartment to another. In general, SNAREs on cargo-carrying vesicles are known as v-SNAREs (also called R-SNAREs due to conserved arginines) and those on the destination or target membranes are called t-SNAREs (also called Q-SNAREs due to conserved glutamines). There are large families of both v- and t-SNAREs, all of which contain at least one amphipathic, helical domain that forms a four helical bundle with other SNAREs. This heteromeric complex spans the two membranes to promote lipid mixing for membrane fusion and cargo transfer. Though the significance of their diversity is unclear, certain SNARE combinations (v and t) are optimal for the fusion steps required for specific membrane trafficking steps. For extracellular secretion (exocytosis), t-SNAREs are a heterodimer of syntaxins and SNAP-23/35s. Despite being the minimal components required for fusion, in order for SNAREs to mediate physiologically significant processes, they must be controlled by regulators and post-translational modifications. The regulators affect, where, when, and how fast membrane fusion occurs. Most of the regulators affect the t-SNAREs. Syntaxins are controlled by chaperones of the Sec1/Munc18 (SM) family, which not only stabilize the syntaxins but also guide their binding to other SNAREs. SNARE-23/25s are dynamically anchored in the membranes via thioester-linked acyl groups. SNAP-23 also appears to be acutely controlled by phosphorylation. Regulation of the v-SNAREs appears less wide-spread. Several SNARE accessory proteins have C2 domains that enable calcium-dependent, membrane binding to acidic lipids. Syntaptotagmins are membrane proteins on vesicles thought

to be key, calcium sensors that, together with complexins, control the final steps of membrane fusion. Other C2 domain-containing proteins, *e.g.*, Munc13 family members, are docking factors that bring the two membranes together to engage the SNAREs for subsequent vesicle-target membrane fusion. The Munc13 proteins work with small GTP-binding proteins, called Rabs, to promote docking. Together the SNAREs and SNARE regulators mediate the highly controlled membrane fusion events that underlie many diverse processes such as neurotransmission, hormonal regulation, and hemostasis.

**Key Words:** Munc, secretion, SNAREs

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#### **0191 Signaling endosomes and epithelial**

**morphogenesis.** C. D'Souza-Schorey\*,  
*University of Notre Dame, Notre Dame, IN.*

Tumor development in glandular tissues is associated with structural alterations in the hollow ducts and spherical structures that comprise such tissues. We have described a signaling axis that provokes dramatic changes in the organization of epithelial cysts, reminiscent of tumorigenic glandular phenotypes. In reconstituted basement membrane cultures of renal epithelial cysts, enhanced activation ARF6 (ADP-ribosylation factor 6) downstream of receptor tyrosine kinases induces the formation of cell-filled glandular structures with aberrant phenotypes. All of these alterations are accompanied by growth factor receptor internalization into signaling endosomes and reversed by blocking ARF6 activation or receptor endocytosis. Receptor localization in signaling endosomes results in hyperactive extracellular signal-regulated kinase signaling leading to abnormal cellular alterations. These findings identify a link between ARF6-regulated receptor internalization and events that drive dramatic alterations in epithelial glandular morphogenesis providing new mechanistic insight into the molecular processes that can promote epithelial glandular disruption.

**Key Words:** ARF6, epithelial morphogenesis, signaling endosomes

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#### **0192 Structural and signaling functions of sphingomyelinases during inflammation.**

M. N. Nikolova-Karakashian\*, *University of Kentucky, Lexington.*

Sphingolipids are lipid molecules with structural, signaling, and metabolic functions. Sphingomyelinases (SMases) convert sphingomyelin, a mostly structural lipid, to ceramide, a bioactive metabolite. Two of the five known SMases play distinct roles in inflammation. Neutral sphingomyelinase-2 (nSMase-2) is a plasma membrane-localized enzyme and mediates the hepatocyte response to IL-1b. Our experiments have identified PP2A, IRAK1, JNK, FoxO1, and the insulin-like growth factor binding protein 1 (IGFBP1) as components of a novel pathway in the IL-1b signaling network that are dependent on nSMase-2. Surprisingly, we also found that

conditions associated with chronic, subclinical inflammation (like oxidative stress, hepatic steatosis, and aging), affect the basal activity of nSMase2, causing up-regulation of that specific pathway and IL-1b hyperresponse. Experiments in mice and rats also show that silencing of nSMase-2 in hepatocytes can be achieved in vivo and can help alleviate an exacerbated IL-1b response.

Acid sphingomyelinase (ASMase) is localized in the endo-lysosomal compartment of the cells and impacts the dynamics of lipid raft domains and endosomes. These effects are especially important for the functions of macrophages during the innate immune response. In activated macrophages, ASMase activity modulates the magnitude of LPS-induced secretion of TNFa. The mechanism is complex and involves the regulation of: (1) the activity of TACE, an enzyme that cleaves the inactive TNFa precursor (pro-TNFa) to its active form and (2) the rate of recycling of pro-TNFa between lysosomes and the plasma membrane. Together, these experiments delineate a novel understanding of the bioactive functions of SMases in chronic and acute inflammation.

**Key Words:** inflammation, liver, macrophage

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**0193 Practical application of the basic aspects of membrane trafficking and receptor-mediated signaling on issues related to animal agriculture.**

S. B. Smith\*, *Texas A&M University, College Station.*

Because of the relatively short life spans of beef cattle, membrane trafficking in relation to inflammation is not considered important unless it overtly affects productivity. However, glucose uptake and utilization is important for adipose tissue development in beef cattle, and increasing glucose utilization in intramuscular adipose tissue can increase carcass quality. Research from the 1980s demonstrated a lack of insulin sensitivity in isolated bovine adipocytes and adipose tissue explants incubated in vitro. Insulin did not stimulate glucose or acetate incorporation into fatty acids, nor did it increase concentrations of glycolytic intermediates in bovine adipose tissue incubated with exogenous glucose. Specific binding of [I125] iodinsulin and insulin degradation in bovine isolated adipocytes was low to non-detectable. These early studies indicated that insulin-dependent receptor-mediated signaling was less important in bovine adipose tissue than in adipose tissues of humans or laboratory species. Recent research demonstrated that GLUT4 expression in muscle and adipose tissue declined markedly after birth in calves, indicating the development of insulin resistance as cattle transitioned from suckling to functional ruminants. Insulin resistance is important in dairy cattle, and causes ketosis and fatty liver. In dairy cattle, s.c. adipose tissue GLUT4 expression decreased 50% following parturition, although insulin responsiveness in s.c. adipose tissue was restored as early as 3 wk postpartum. Expression of genes associated with insulin responsiveness (*IRS1*, *INSIG2*, *SREBF1*, and *ZFP423*) was upregulated in similar fashion.

Understanding the underlying mechanisms of insulin resistance and inflammation would increase animal health and thereby improve productivity.

**Key Words:** adipose tissue, bovine, insulin

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**ASAS GRADUATE STUDENT SYMPOSIUM**

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**0194 Marketing 101: Learning how to market yourself for a successful career.** R. M. Yamka\*, *Blue Buffalo Company Ltd., Wilton, CT.*

The animal science industry can be a competitive marketplace as new graduates begin to look for a new job. Having good grades, the right skill set (laboratory experience, publication experience, good grades, etc.) and work experience (collecting samples, computer experience, working with animals, etc.) is not always enough to secure employment. Especially in a competitive job market. As a result, identifying ways to stand out from the crowd becomes important. Unfortunately, most job candidates do not realize that it is important to learn how to market and sell yourself to your target audience to meet their current and future business goals. How you market and sell yourself will be career and industry dependent (academia vs. consumer goods vs. pharma). Marketing and selling yourself does not end once you get your foot in the door. Marketing and selling yourself continues as you advance in your career. Although it is not as formal as the interview, marketing yourself requires you to network, communicate and engage management inside & outside your department. In addition, looking for new opportunities to build your credentials (board certification, become the "go to" person) and identifying ways to be unique will help set you apart and differentiate you from your peers. In this session, some of these key strategies will be discussed and how they can be applied for a successful career.

**Key Words:** marketing yourself, target audience, successful career, professional development

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**0195 Personal branding.** M. Calvo-Lorenzo\*, *Elanco Animal Health, Greenfield, IN.*

Who you are and how you carry yourself are very important to becoming successful. As a student and professional, your personal brand keeps you current in your own field, opens doors of opportunities for you, and creates a lasting impression. While making an unforgettable first impression in person is important, it is no longer the only way to establish your brand. Personal branding should help individuals define themselves in their workspace, while also incorporating the personal elements that make you who you are. In this session, several strategies will be discussed on creating a successful personal brand, while providing an overview on how to articulate one's