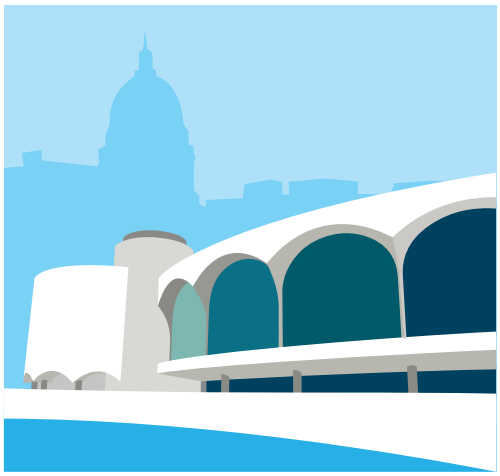
A first insight into the effect of Lotilaner on GABA-gated channels from the european tick Ixodes ricinus

Claude Charvet, Clément Auger, Claude Rispe, Caroline Hervet, Elise Courtot, Steeve Thany, Olivier Plantard, Cédric Neveu



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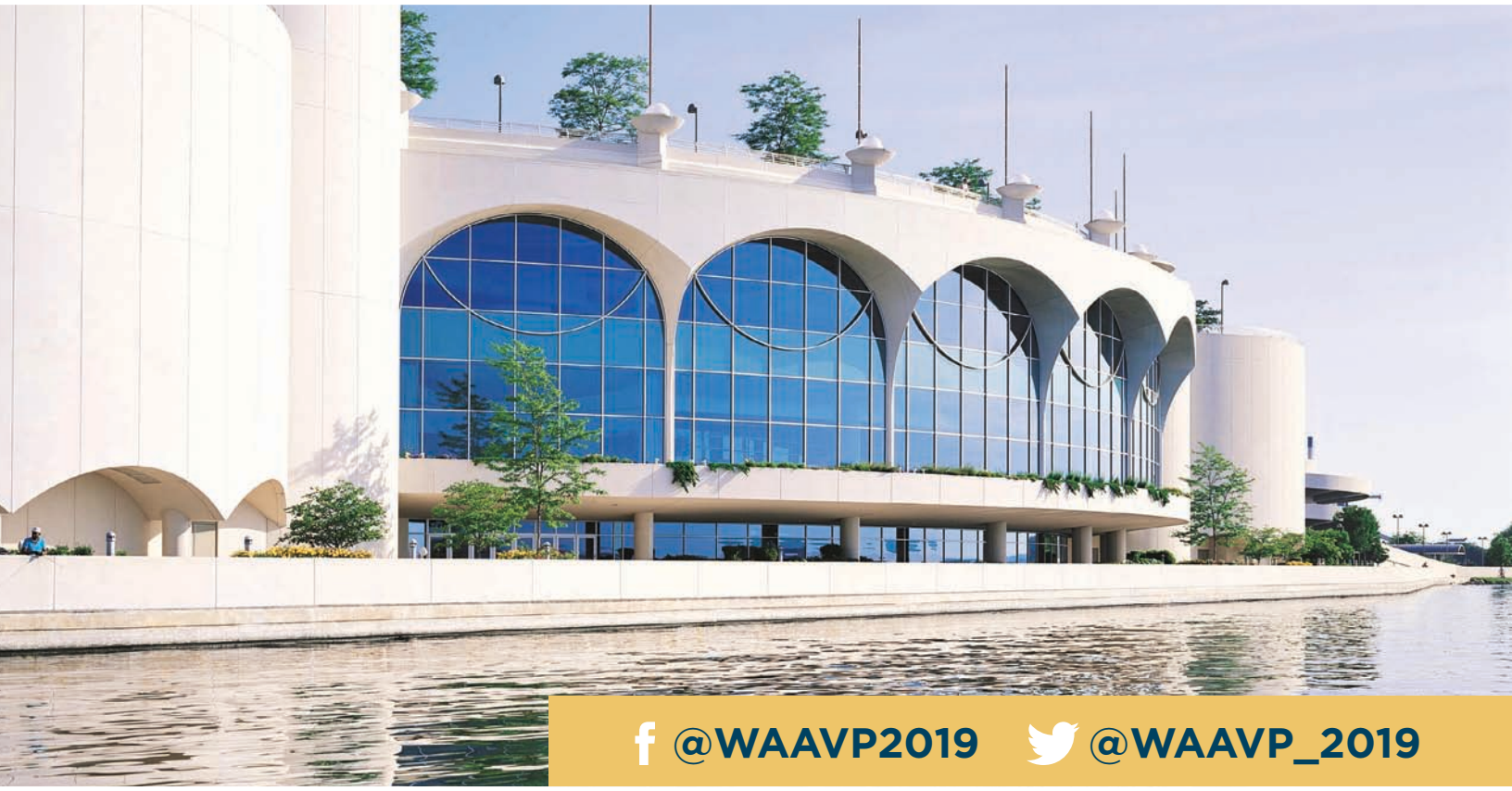

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humidity). Geometric means of combined live tick counts were calculated for attachment intervals of 1–2 hours, 3–4 hours, 5–6 hours, and 7–8 hours, and least squares means were compared by ANOVA with a two-sided significance level set at α=0.05. Significantly fewer live I. scapularis were removed from treated than control dogs after 3–4 hours of attachment (p=0.0012); upon holding 24 hours, significantly fewer I. scapularis that had previously been attached to treated dogs for 1–2 hours were alive (p=0.0049). Significantly fewer live A. americanum were removed from treated than control dogs after 7–8 hours of attachment (p=0.0254); upon holding 24 hours, significantly fewer A. americanum that had previously been attached to treated dogs for 3–4 hours were alive (p=0.0003). These data indicate that acaricidal activity of sarolaner against I. scapularis and A. americanum begins after 1–2 hours and 3–4 hours of attachment, respectively, on sarolaner treated dogs.

OA13.04 A First Insight Into the Effect of Lotilaner on GABA-Gated Channels From the European Tick Ixodes Ricinus

Dr Claude Charvet[1], Clément Auger[1], Dr Claude Rispe[2], Caroline Hervet[2], Dr Elise Courtot[1], Pr Steeve Thany[3], Dr Olivier Plantard[2], Dr Cédric Neveu[1]
[1]INRA, ISP, Université Tours, UMR1282, Nouzilly, France, [2]INRA, Oniris, BIOEPAR, Nantes, France, [3]Université d'Orléans, LBLGC, USC1328 INRA, Orléans, France

Ticks are strict blood-feeding arthropods (Acari), which represent a major health issue for wild or domesticated animals and humans, due to their potential to transmit disease agents. Control of ticks is increasingly difficult due to the development of drug-resistant parasites. Ligand-gated ion channels of the tick central nervous system are the primary targets of acaricides. Among those receptors, the γ-aminobutyric acid-gated chloride ion channels (GABACIs) are the main synaptic inhibitory receptors. Lotilaner is a recently developed parasiticide from the isoxazoline chemical class that was shown to be a non-competitive antagonist of GABACIs from the livestock tick Rhipicephalus microplus. In the present study, we characterized the GABACIs from the European tick species Ixodes ricinus.

We extracted RNAs from Ixodes ricinus nymphs. Taking advantage of the phylogenetic closeness of I. ricinus and R. microplus in the Arthropoda phylum, we identified the I. ricinus GABACl subunit homologue. The cDNA encoding the Iri-GABACl was cloned and the corresponding in vitro synthesized cRNAs were micro-injected into Xenopus laevis oocytes to investigate its pharmacological properties. Functional expression and two-electrode voltage clamp studies demonstrated that the GABACl subunit formed a homomeric receptor gated by GABA. Importantly, the insecticides like lotilaner, fipronil and picrotoxin efficiently blocked the GABA currents as previously observed for the R. microplus GABACl. Surprisingly, I. ricinus GABACl was not sensitive to the pesticide dieldrin, suggesting a potential naturally existing resistance mechanism involving alternative exons.

Here we report the functional characterization of the first GABACl of I. ricinus demonstrating that it is an important molecular target for lotilaner. Transcriptomic analysis of I. ricinus are in progress to identify new acaricidal targets.

OA13.05 Clinical Efficacy of Afoxolaner in Dogs Naturally Infected With Sarcoptes Scabiei and Concomitant Modifications of the Skin Microbiota

Raluca Mindru[2], Andrei Cristian Lupu[2], Dr. Constantin Roman[2], Dr. Charlotte Bernigaud[5], Dr. Amaury Briand[1], Dr. Frédéric Beugnet[3], Dr. Katja Fischer[4], Professor Liviu Miron[2], **Professor Jacques Guillot**[1]
[1]Veterinary College of Alfort, Maisons-alfort, France, [2]Ion Ionescu de la Brad, Faculty of Veterinary Medicine, Iasi, Romania, [3]Boehringer Ingelheim Animal Health, Lyon, France, [4]QIMR Berghofer, Medical Research Institute, Brisbane, Australia, [5]Henri Mondor Hospital, France

Infection by Sarcoptes scabiei remains a common disease in dogs, especially in tropical countries where most of stray or non-controlled dogs show cutaneous