Evaluation of Hemorrhage and Edema Expansion, Including Effect on Neutrophil-Mediated Neuroinflammation in Intracerebral Hemorrhage, Using Ir-CPI, a Thromboinflammation Inhibitor

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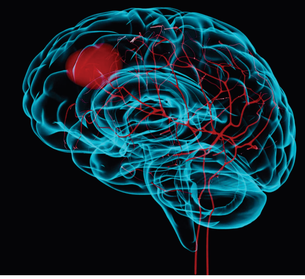

Ir-CPI, a breakthrough drug candidate for intracerebral hemorrhage

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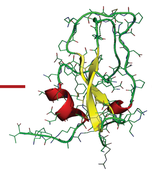
INTRODUCTION

Intracerebral hemorrhage (ICH) is a subtype of stroke with a high mortality and functional disability rate.

The inflammation and coagulation responses after ICH would accelerate the formation of perihematomal edema, resulting in brain herniation-related death and **neurological deficits**. Patients with ICH also frequently present with **thrombotic events**. However, **medical treatments** for inflammation and safe prevention of thrombosis **are lacking** during the hyperacute phase of ICH.

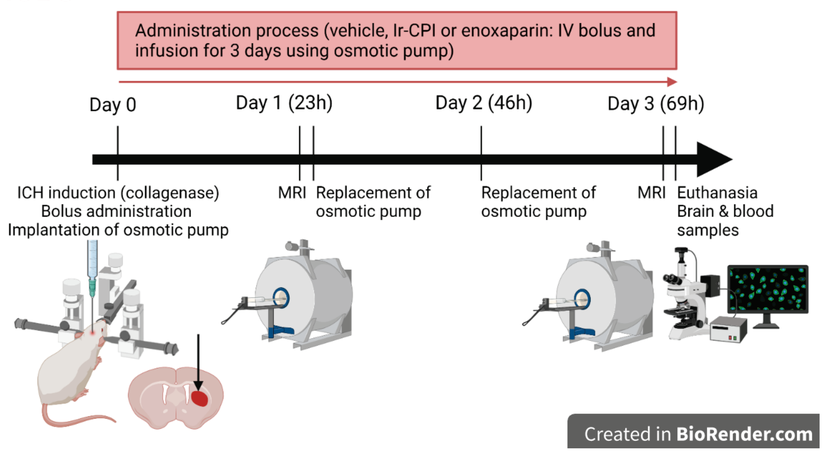
Ir-CPI, a protein isolated from the salivary glands of the tick *I. ricinus*, is an inhibitor of **coagulation factors** FXIIa and FXIa and **neutrophils**, with proven antithrombotic and anti-inflammatory effects in various animal models[1,2].

Coagulation Factors XIIa & FXIa ⊣  ⊣ Neutrophils & NET release

AIMS

To evaluate the effects of Ir-CPI, in a mouse model of ICH, on evolution of perihematomal edema and hemorrhage volumes, **neutrophil infiltration** (incl. the release of NETs) and **neuronal degeneration**.

METHODS



RESULTS

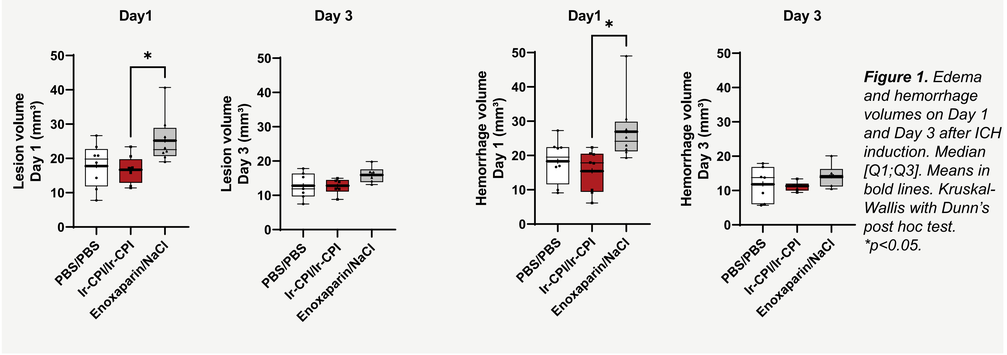


Figure 1. *Edema and hemorrhage volumes on Day 1 and Day 3 after ICH induction. Median [Q1;Q3]. Means in bold lines. Kruskal-Wallis with Dunn's post hoc test. *p<0.05.*

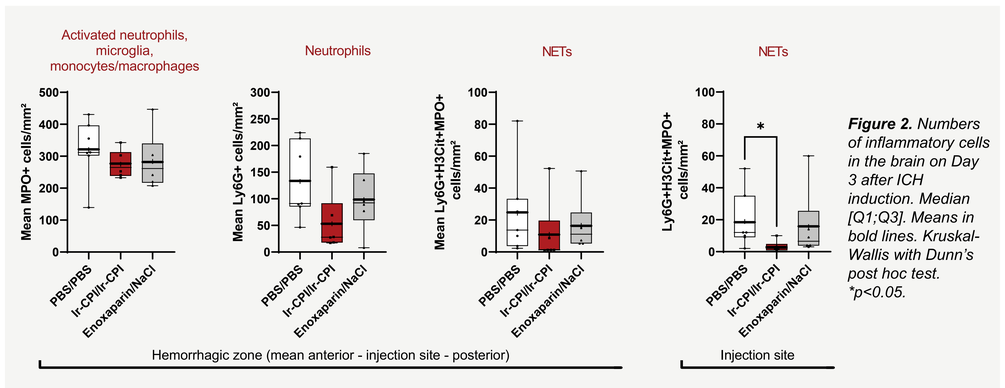


Figure 2. *Numbers of inflammatory cells in the brain on Day 3 after ICH induction. Median [Q1;Q3]. Means in bold lines. Kruskal-Wallis with Dunn's post hoc test. *p<0.05.*

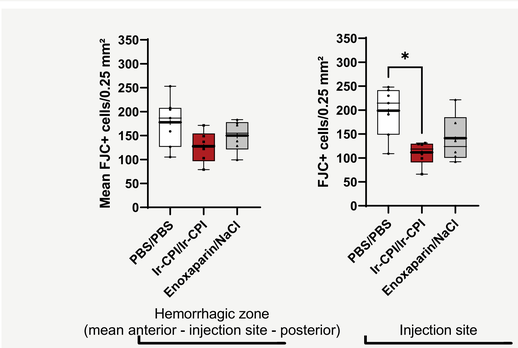


Figure 3*. Numbers of degenerating neurons on Day 3 after ICH induction. Median [Q1;Q3]. Means in bold lines. Kruskal-Wallis with Dunn's post hoc test. *p<0.05.*

CONCLUSION

Administration of Ir-CPI in mice post-ICH induction:

- ✓ is **safe**,
- ✓ **reduces neutrophil infiltration** including neutrophil-releasing NETs, &
- ✓ **attenuates neuronal degeneration**.

REFERENCES

[1]Decrem, Y., et al. Ir-CPI, a coagulation contact phase inhibitor from the tick Ixodes ricinus, inhibits thrombus formation without impairing hemostasis. J Exp Med 206, 2381-2395 (2009).

[2]Pireaux, V., et al. Anticoagulation With an Inhibitor of Factors XIa and XIIa During Cardiopulmonary Bypass. J Am Coll Cardiol 74, 2178-2189 (2019).

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Avec le soutien de la Wallonie