



Aim Does circulating HBsAg induce tolerance?



Decoy for anti-HBsAg Antibodies

Induction of Immune Tolerance

Boni et. al., Gastroenterology, 2012 Zhou et al., J immunol, 2016 Bazinet et al., Gastroenterology, 2020



Methods Mouse models to study immune-mediated HBV pathogenesis



Methods

Models to study the role of circulating HBsAg in affecting CD8⁺ T cell response



A fraction of HBV replication competent transgenic mice spontaneously clear serum HBsAg

Spontaneous HBsAg loss



HBsAg clearance does not cause overt reactivation of tolerant T cells present in HBV Tg mice









HBsAg clearance has minimal impact on HBV-specific CD8⁺ T cell responses



HBsAg clearance has minimal impact on HBV-specific CD8⁺ T cell responses









HBsAg has no impact on the capacity of HBV-effector CD8⁺ T cell to induce liver immunopathology

HBsAg has minimal effect on HBV-CD8⁺ T cell expansion without affecting their differentiation in dysfunctional cells

Same results were obtained upon anti-HBsAb treatment to reduce HBsAg levels

CD8⁺ T cells

CD8⁺ T cells

Functional improvement of intrahepatically primed CD8⁺ T cells by IL-2 based immunotherapeutic strategies

Analyses

Х

**

PBS

IL-2c

Х

(dav 5)



PBS

IL-2c

Circulating HBsAg does not affect the functional improvement of intrahepatically primed CD8⁺ T cells by IL-2 based immunotherapeutic strategies



HBV-specific TCR CD8⁺ T NAÏVE cells Dysfunctional response

Benechet, De Simone et al., Nature, 2019

IL-2 based therapy





HBsAg clearance do not improve the functional restoration of intrahepatically primed CD8⁺ T cells by IL-2-based immunotherapeutic strategies

Conclusion HBV-specific CD8⁺ T cell response is not affected by the levels of circulating HBsAg



Initial hypothesis

HBsAg clearance



13

Conclusion HBV-specific CD8⁺ T cell response is not affected by the levels of circulating HBsAg



Acknowledgments



San Raffaele Scientific Institute



Matteo Iannacone Luca Guidotti

Pietro Di Lucia Valentina Venzin Elisa B.Bono Leonardo Giustini Mirela Kuka **Cristian Beccaria** Micol Rava' Federica Moalli Marta Grillo Francesco Andreata Xenia Ficht Davide Marotta Chiara Perucchini Mattia Freschi Eleonora Sala **Bianca** Partini Chiara Laura Caroline Kruger Elena Rodriguez Keigo Kawashima Marta Mainetti



The Scripps Research Institute

Francis V. Chisari

Gilead Sciences Robert Jordan William Delaney