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Creating Cross-Reactive Antibodies to Detect and Treat Synthetic Cannabinoid Receptor Agonist Toxicity

Maobing Tu*

Department of science, Auburn University, School of Forestry and Wildlife Sciences, USA

Introduction

The pharmacology of the psychotropic elements in cannabis is mimicked by substances known as synthetic cannabinoid receptor agonists (SCRAs). These substances are readily available for recreational use because they have a wide range of structural variations, are affordable, readily available commercially, and are challenging to identify using current analytical techniques. Symptom management is currently used to treat suspected SCRA poisoning, which can manifest as a variety of cardiovascular, gastrointestinal, and neurological disorders. This is followed by a toxicological screening, which frequently takes place a long time after the patient has been discharged [1].

Description

It was discovered that the antibodies produced by vaccination with these bio conjugates demonstrated their capacity to detect multiple SCRAs with a Tanimoto minimum common structure score of 0.6 or greater, at concentrations below 8 ng/mL, using a combination of multiplexed competitive ELISA screening and chemoinformatic analyses. It was discovered that the range of SCRAs detectable utilising these haptens included both bioisosteric and non-bioisosteric variants within the core and tail subregions, as well as SCRAs containing valine-like head sub regions, which are unaddressed by commercially available ELISA screening techniques [2].

Novel psychoactive compounds are synthetic versions of medicines that cause psychotropic effects via mechanisms in the central nervous system (NPS). Opioid and serotonin receptor agonists are two traditional categories of NPS that have recently been expanded to include cannabinoid 1 receptor (CB1R) agonists as well. Synthetic cannabinoid receptor agonists (SCRA) are the fastest-growing class of NPS while being relatively new. To date, over 260 different compounds have been identified as SCRA. related metabolites, with high accuracy.These practical considerations, which are probably amplified in environments with limited resources, offer a compelling case for the continued development of immunologic, enzyme-linked immunosorbent assay (ELISA)-based approaches as a less expensive, more widely available method for real-time SCRA detection. A particular feature of antibody-based screening methods that cannot be matched by LC-MS methods is their potential to be used in therapeutic interventions, such as monoclonal infusion for overdose reversal [3].

In an effort to evaluate both the significant structural variations that can exist within the head sub region as well as the more subtle modifications frequently found within the core and linker sub regions, our investigation into the development of a wider spectrum of cross-reactive anti-SCRA antibodies started with the synthesis of four haptens. The biological significance of inoculation was evaluated following bio conjugation and vaccine formulation by administering structurally similar SCRAs, which cause a consistent pattern of quantifiable physiological changes.

Such improvements in knowledge of novel SCRA cross-reactivity immunopharmacological methods for identifying and reducing their effects may also result in a more thorough comprehension of the connection between haptenic structure and antibody function for additional clinically significant NPS classes. Finally, despite the fact that pre-success immunization's in preventing SCRA effects in vivo is a promising proof of concept, this preventative strategy is unlikely to have therapeutic applicability. To maximize both their diagnostic and therapeutic potential, it is essential to develop optimal monoclonal anti-SCRA antibodies [4].

This study discusses the synthesis of four haptens, three of which were able to produce strong anti-SCRA antibody titers with micromolar to sub micromolar affinities against various SCRA compounds with an MCS structural similarity score of 0.6 or above, in comparison to the hapten itself. As a result, several structurally similar SCRAs, including more recent generations of SCRAs that are undetectable by current commercial ELISA kits, were detected widely at concentrations below 10 ng/mL. By demonstrating functional inhibition of SCRA-induced toxicologic effects in mice at dosages of 1-3 mg/kg, the polyclonal sera created in this work were also able to demonstrate the feasibility of using antibody-based methods for symptom relief in the context of SCRA toxicity [5].

Conclusion

These results serve as a foundation for the further development of multiplexed SCRA ELISA screening panels, which can deliver useful information about SCRA generational and structural identity in minutes to hours rather than days to weeks. This information is particularly pertinent in light of the growing number of SCRA analogues that are otherwise unidentified or cryptic. Based on the ability of the anti-SCRA antibodies described here to mitigate the adverse effects of SCRAs, it is possible to add value by combining this multiplexed screening strategy with the creation of monoclonal antibodies for quick SCRA overdose reversal in order to produce an integrated rapid detection and intervention platform to handle upcoming SCRA intoxication outbreaks.

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***Address for Correspondence:** Maobing Tu, Department of science, Auburn University, School of Forestry and Wildlife Sciences, USA; E-mail: maobingtu@outlook.com*

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