The clinical course of anti-p200 pemphigoid is variable. In contrast to epidermolysis bullosa acquisita and bullous pemphigoid, what is concerned here is a relatively benign disease with a good therapeutic response. Therefore, it is of great clinical importance to differentiate between these diseases.

US6,682,911 discloses laminin 12 and preparations of isolated laminin 12 and of subunits thereof.

Against this background, there is a need for a detection procedure for anti-p200 pemphigoid that has higher diagnostic reliability, especially sensitivity. At the same time, there is the additional aim of improving the differentiability between the various blistering autoimmune diseases of the skin.

Summary

In a first aspect, the object underlying the disclosure is achieved by a polypeptide comprising laminin beta-4 or a variant thereof, preferably in recombinant and/or isolated form.

In a preferred example, the polypeptide is immobilized.

In a second example, the object is achieved by a carrier comprising the polypeptide according to the disclosure, and further comprising at least one antigen, preferably all the antigens, from the group comprising laminin gamma-1, BP180, BP230, desmoglein 1, desmoglein 3, envoplakin, deamidated gliadin, laminin 332 and collagen type VII or variants thereof.

In a preferred example, the carrier is selected from the group comprising a glass slide, preferably slide for microscopy, a biochip, a microtiter plate, a lateral flow device, a test strip, a membrane, preferably a blot, more preferably a line blot, a chromatography column material and a bead, preferably a magnetic or fluorescent bead.

In another aspect, the object is achieved by a therapeutically useful carrier comprising the polypeptide according to the disclousre, wherein the carrier allows the contacting of human blood with the polypeptide followed by the recirculation of the blood into the body of a patient, the carrier preferably being an apheresis apparatus.

In another aspect, the object is achieved by an antibody, preferably autoantibody, against laminin beta-4, preferably in isolated form.

In another aspect, the object is achieved by the use of the polypeptide, carrier or autoantibody according to the disclosure for the diagnosis of a disease.

In another aspect, the object is achieved by a method for producing a diagnostically or therapeutically useful carrier, comprising the step of coating the carrier with the polypeptide according to the disclosure.

In yet another aspect, the object is achieved by a method for purifying an autoantibody, comprising the steps of a) contacting a liquid comprising the autoantibody with the polypeptide according to the disclosure under conditions which allow the formation of a complex comprising the autoantibody and the polypeptide, b) isolating the complex from step a), and c) optionally detecting the complex from step a) or dissociating the complex isolated in step b) followed by removal of the autoantibody from the polypeptide.

In yet another aspect, the object is achieved by a method comprising the step of detecting an autoantibody against laminin beta-4 in a sample.

In a further aspect, the object is achieved by a pharmaceutical composition comprising the polypeptide according to the disclosure or a variant thereof, preferably together with a pharmaceutically acceptable carrier.

In a further aspect, the object is achieved by a kit comprising the polypeptide according to the disclosure or the carrier according to the disclosure, wherein the kit contains one reagent or more than one reagent, preferably all the reagents, from the group comprising a wash solution, a calibrator solution, an antibody against laminin beta-4, and an agent for the detection of an autoantibody against laminin beta-4, preferably a secondary antibody.

In an example, the object is achieved by the use of the polypeptide according to the disclosure, of the carrier according to the disclosure or of an antibody, preferably autoantibody, against laminin beta-4 for the production of a kit or diagnostically or therapeutically useful carrier.

In a preferred example, an autoantibody against laminin beta-4 is detected using a method selected from the group comprising immunodiffusion, immunoelectrophoresis, light scattering, agglutination, immunoassay with labeling such as that from the group comprising immunoassay with radioactive labeling, with enzymatic labeling, more preferably ELISA, with chemiluminescence labeling, more preferably electrochemiluminescence labeling, and with immunofluorescence labeling, preferably indirect immunofluorescence.

In another example, the object is achieved by the use of the polypeptide according to the disclosure or of the antibody according to the disclosure for the determination of the capability, preferably capacity, of a diagnostic or therapeutic device or of a diagnostic or therapeutic reagent to bind an antibody against laminin beta-4.

The present invention is based on the surprising finding by the inventors that an autoantibody against laminin beta-4 exists and can be specifically detected in patients who suffer from anti-p200 pemphigoid.

The inventors further found that the detection of said autoantibody increases the sensitivity of the serological diagnostic assay for anti-p200 pemphigoid. It can be detected in some patients in whom it is not possible to detect the autoantibody against laminin gamma-1, which autoantibody was hitherto considered to be of sole importance.

Laminins are trimeric basal membrane proteins which consist of alpha, beta and gamma chains. Laminin beta-4 is a beta chain. Laminins are involved in many physiological functions such as, for example, cell adhesion, migration, differentiation, neuronal development and in the regulation of gene expression.

Choi *et al*. (2015) observed a reduced expression of laminin beta-4 in cancer tissue of the stomach and intestine. They identified somatic laminin beta-4 mutations in cancer tissue that possibly contributed to a reduced expression of laminin beta-4 (Choi, M. R., An, C. H., Yoo, N. J., Lee, S. H. Laminin gene LAMB4 is somatically mutated and expressionally altered in gastric and colorectal cancers. APMIS 123: 65-71, 2015). Moreover, reduced levels of laminin beta-4 might also play a role in diverticulitis (Coble JL, Sheldon KE, Yue F, Salameh TJ, Harris LR III, Deiling S, Ruggiero FM, Eshelman MA, Yochum GS, Koltun WA, Gerhard GS, Broach JR. Identification of a rare LAMB4 variant associated with familial diverticulitis through exome sequencing. Hum Mol Genet. 2017; 26(16): 3212-3220).

The present invention provides a polypeptide comprising a mammalian laminin beta-4, preferably from humans, simians, cattle, sheep or pigs and particularly preferably from humans.