La brevetabilité des anticorps des deux côtés de l'Atlantique : point sur la situation en Europe

12 juin 2018

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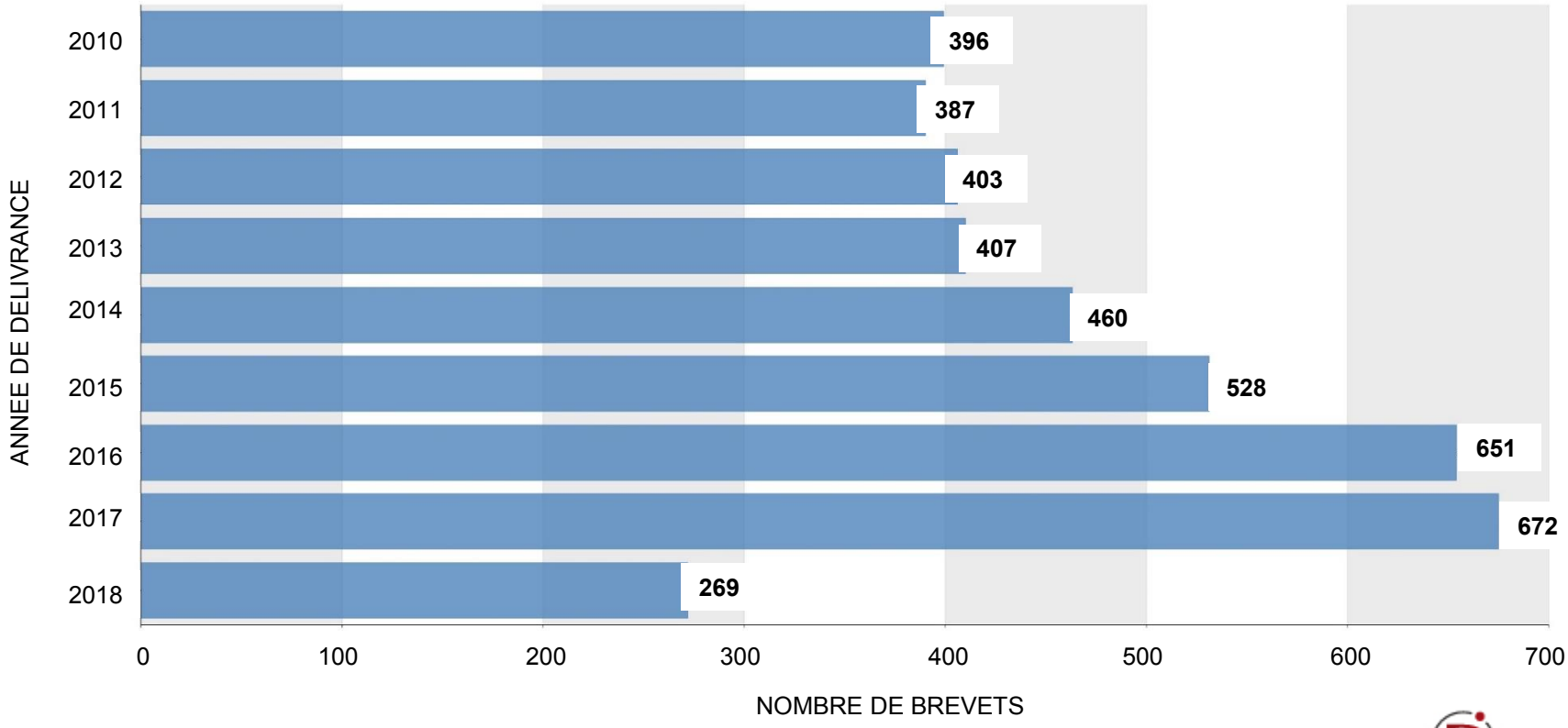
Associée

Introduction

- Brevets EP délivrés depuis 2010



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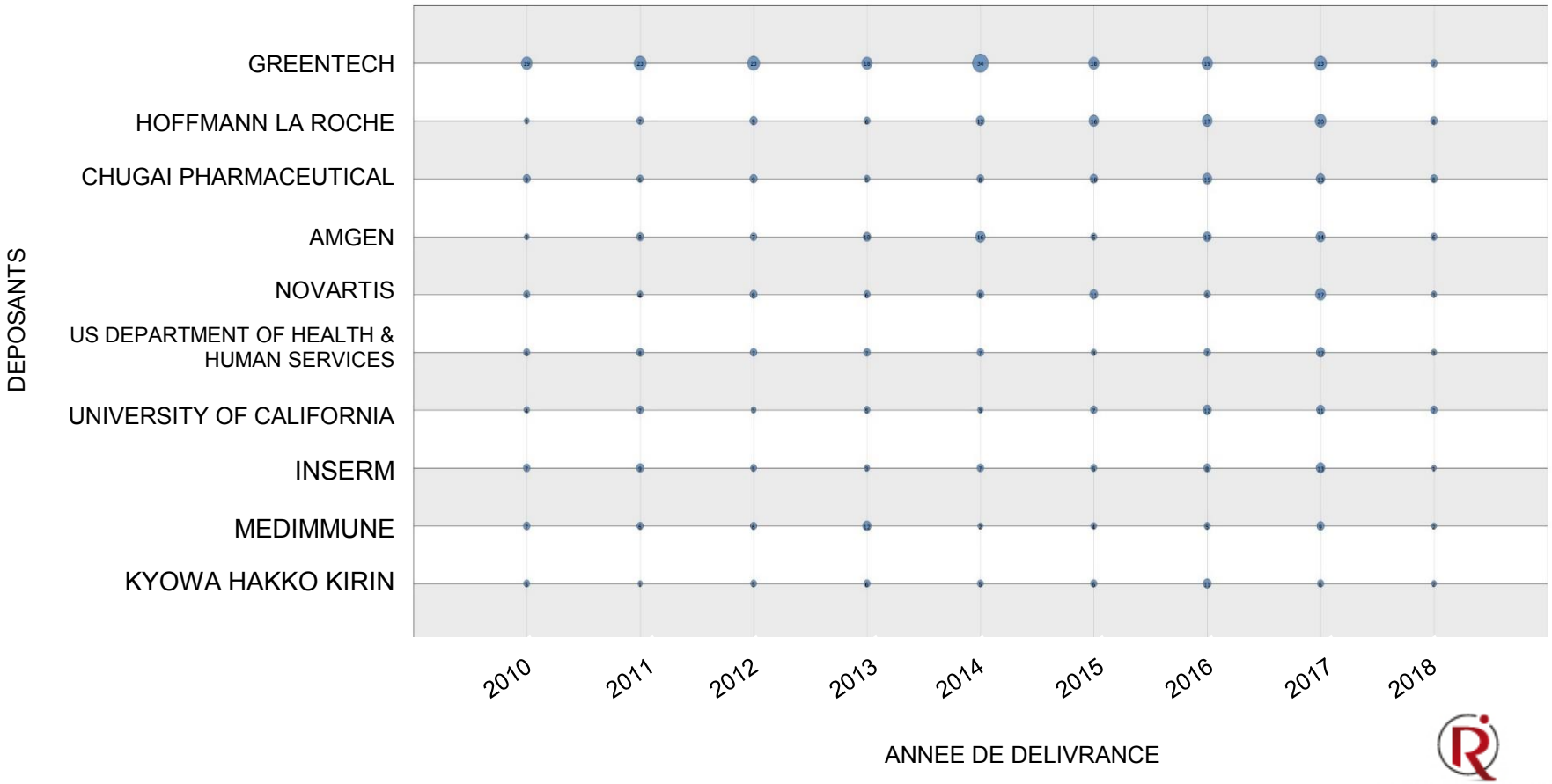
Introduction

- Top 10 déposants - Brevets EP délivrés depuis 2010



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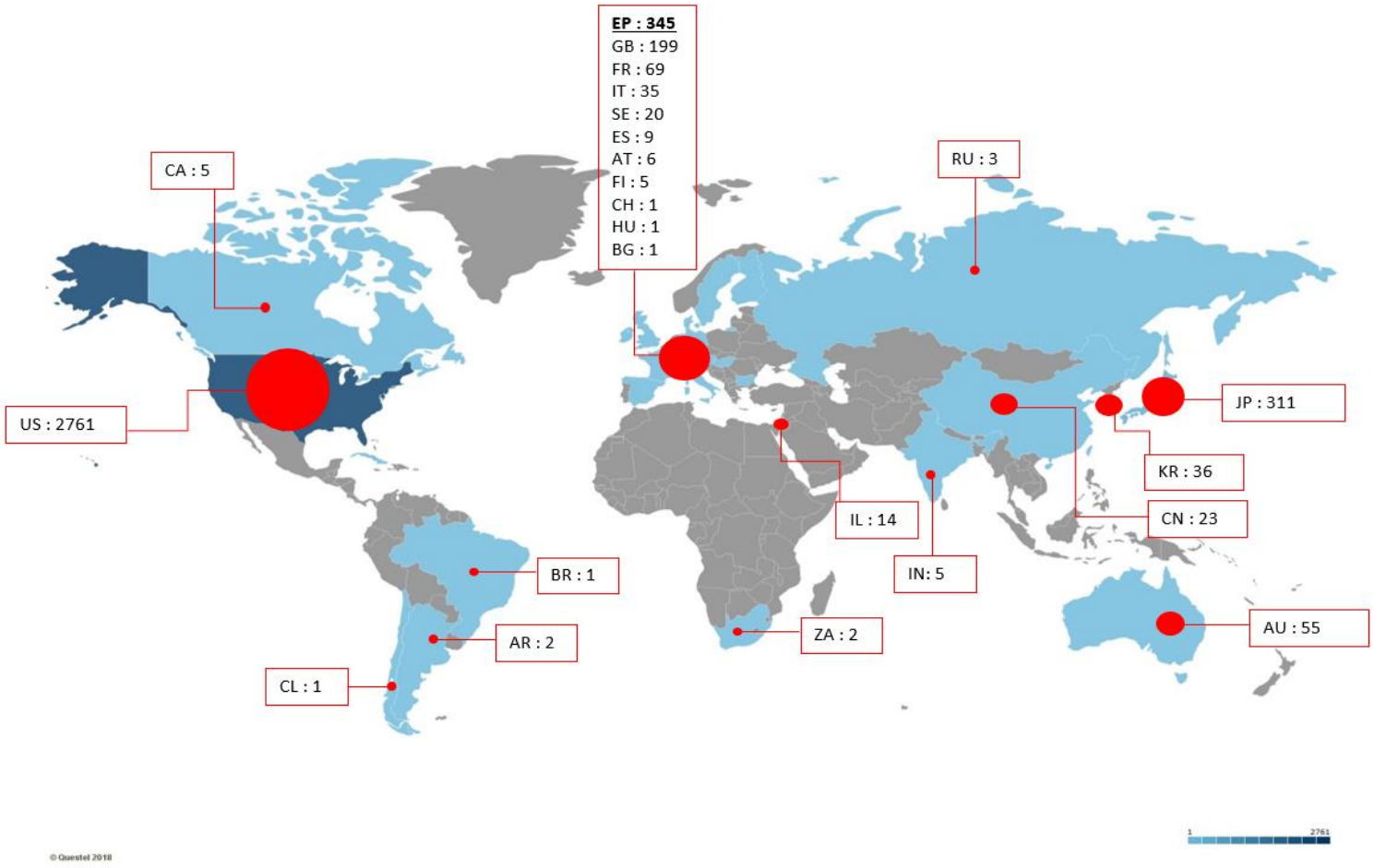
Introduction

- Pays de priorité - Brevets EP délivrés depuis 2010



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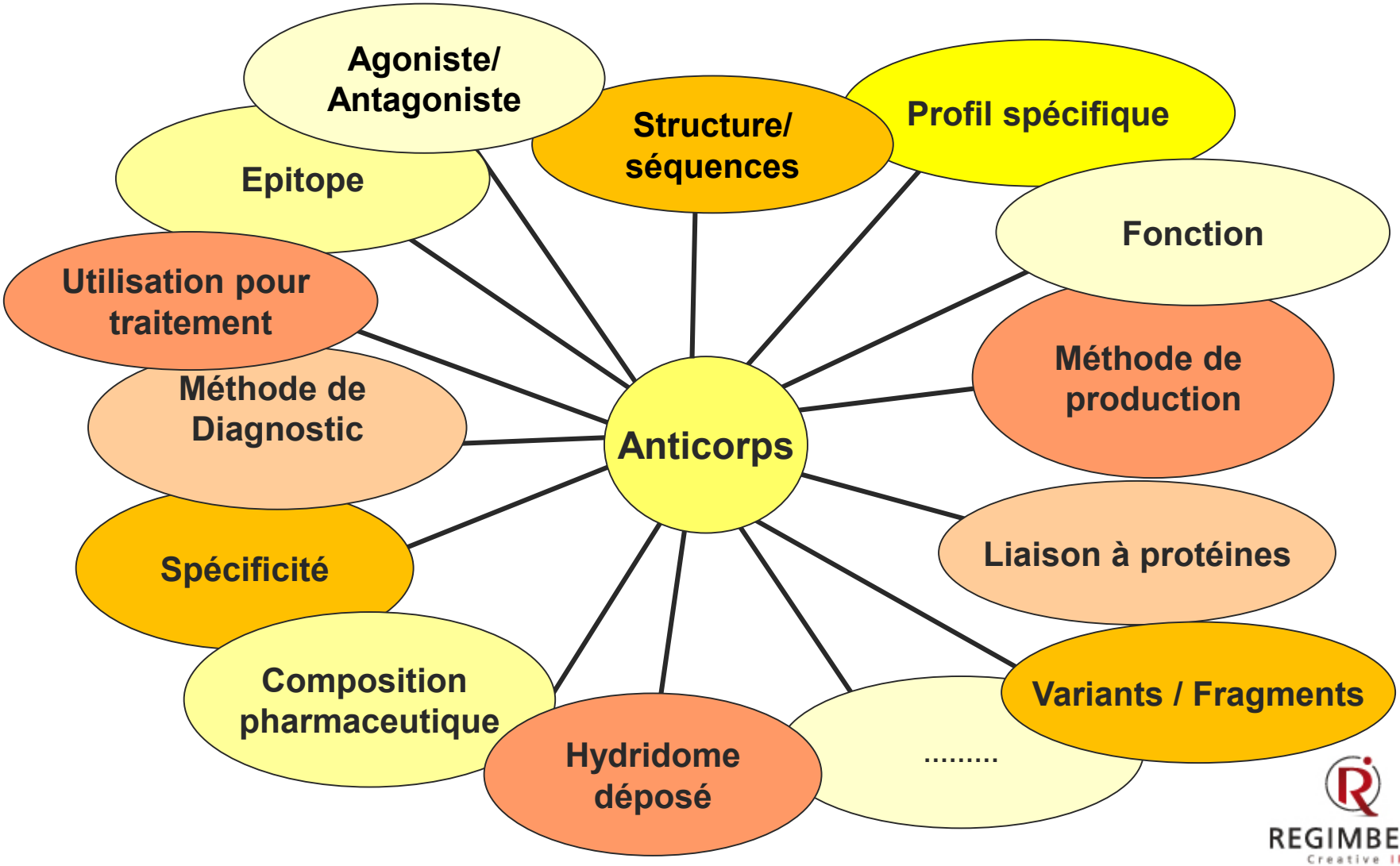
Anticorps : aspects brevetables



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Brevetabilité des anticorps en EP

- Principales problématiques
  - Activité inventive
    - Approche problème-solution
    - État de la technique le plus proche
    - Alternative (pas AI)/ Avantage
  - Suffisance de description
    - Connaissances générales / routine
    - Enseignement des exemples
    - Charge de la preuve
    - Données post publication

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Hybridome – Art 83 CBE : oui

- **T431/96**

  Rev 1 = A monoclonal antibody raised against non-denaturated D-dimer that may be utilised in a method of diagnosis of disseminated intravascular coagulation (DIC) or other thrombotic states using body fluid, such as ….., said monoclonal antibody having the essential characteristic of reactivity with D-dimer and other cross-linked fibrin derivatives and non reactivity with fibrinogen or fibrinogen degradation products inclusive of fragent D and fragment E.

« …. the skilled person seeking to reproduce the invention will have to reproduce monoclonal antibodies by routine methods and test them singly in an assay. This may possibly involve some tedious and time-consuming work but nothing out of the ordinary since the techniques for the production and selection of hybridomas were common routine techniques at the priority date of the patent (i.e. 17 March 1983) » (p.13)

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Hybridome – Art 83 CBE : non

- **T1466/05**

  Rev 1 = An antibody reactive with the pyridinoline in peptide-linkedpyridinoline and not free pyridinoline which is useful in an assay to indicate bone resorption.

« …. *whereas the fact that the method used to prepare monoclonal antibody 51A93 has not been disclosed in the application is not necessarily prejudicial in the context of assessing sufficiency of disclosure in respect to this specific antibody – as the hybridoma which produces this antibody was deposited with a recognised depositary institution not later than the date of filing of the application (cf. Rule 28(1)EPC) – the absence of any directions or a suitable protocol for the preparation of further antibodies as defined in claim 1 raises serious doubts wether the requirements of Article 83 EPC, ie a disclosure of the invention which is sufficiency clear and complete for it to be carried out by a person skilled in the art, are fulfilled in respect of all antibodies encompassed by claim 1.* » *(p.11-12)*

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Hybridome – Art 83 CBE : non

- **T0601/05**

  Rev 1 = A pharmaceutical composition containing a human monoclonal antibody that binds to human tumour necrosis factor alpha on human cell surfaces, and is capable of inhibiting LPS-induced human tumour necrosis factor alpha secretion by human monocyte cells.

*«The uniform opinion at the priority date of the patent in dispute was that antibodies useful for treatment of TNF-related disorders should have a **high affinity** to **soluble** TNF and should be capable of **neutralizing** its activity….*

….the claim is to be interpreted as covering antibodies binding to any kind of TNF with any degree of affinity. The claim thus includes antibodies binding with high affinity to soluble TNF.

The only method disclosed in the patent for the production of human monoclonal antibodies is the so-called hybridoma technique which is based on the Köhler-and-Milstein technique developped in the 1970s for the production of mouse monoclonal antibodies.

There is a large body of evidence before the board suggesting that the hybridoma technology is not suited to producing antibodies binding with high affinity to soluble TNF» (p.24-26)

Hybridome – Art 83 CBE : oui

- **T2045/09**

Rev 1 : An antibody which binds to ErbB3 protein and (i) reduces…and (ii) reduces…..

Rev 8 = An antibody which binds to an epitope bound by the 8B8 antibody obtainable by the hybridoma cell line ATCC n° HB-12070.

«…..The description of the patent in suit discloses sources of ErbB3…, the hybridoma technology….and the cross blocking assay…. Hence the patent in suit provides a complete teaching of the technology required for the skilled person to obtain further antibodies falling within the scope of present claim 8.

…..

In the board's view while the evidence may demonstrate that the preparation of antibodies binding to the epitope of the 8B8 antibody is time-consuming, it does not show that the amount of the time needed for their generation is so high that they could only be produced with undue burden» (p.30)

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Suffisance de description : oui

- **T0617/07**

Rev 20 : Monoclonal antibody, synthetic and biological dérivatives thereof, able to recognise and bind the high affinity tyrosine kinase receptor of NGF (Nerve Growth factor), named TrkA, and act as antagonist for the binding of NGF to TrkA, and which prevents the function activation of TrkA by NGF, and characterised by at least one CDR selected from : light chain CDRs defined by aa 46-55 of SEQ ID No 2, aa 71-77 of SEQ ID No 2 and aa 110-119 if SEQ ID No 2 and heavy chain CDRs defined by aa 176-185 of SEQ ID No 2, aa 200-216 of SEQ ID No 2 and aa 249-262 of SEQ ID No 2.

«There is no doubt that the structural definition in claim 20 includes antibodies that do not have the desired function – the definition encompasses example antibodies that have only one CDR from MNAC13 – but, […] when attempting to rework the invention to which claim 20 is directed the skilled person would on the basis of his/her knowledge be able to avoid non-fuctional variants. Therefore, because the skilled person knows how to achieve antibodies with the desired function on the basis of a particular known antibody he/she is not in the situation of having to sort out non-functional variants in a burdensome manner.» (p.23-24)

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Suffisance de description : non

- **T1602/10**

Rev 1 : A TIM-3 binding molecule wherein the TIM-3 binding molecule is an antibody specific for TIM-3 or is a fragment of an antibody specific for TIM-3, for use in a treatment of cancer in a subject.

«In view of the above it is considered that the skilled person would not have considered that the disclosure of the application makes it plausible that it would be possible to generate a de novo immune response to cancers where there was no established native response. Moreover, the skilled person would not have believed that substancially all cancer types inherently generate a Th1, TIM-3 mediated immune response and be treatable by administration of anti-TIM-3 antibodies. It is noted that the post-published documents submitted by the appellant support this conclusion, […] » (p. 9-10)

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Suffisance de description : non

- **T2094/13**

  Rev 1 : A pharmaceutical composition comprising an antibody to Aß and pharmaceutically acceptable non toxic carrier or diluent, for use in preventing or treating a disease characterised by amyloid deposit in a patient, wherein the isotype of the antibody is human IgG1.

«It is uncontested that the patent in suit does not disclose explicit experimental evidence […..].

It was also common ground between that such evidence was not derivable from any cited prior art document. Under these circumstances, the patent in suit must disclose evidence to the skilled person having due regard of common general knowledge, that compositions comprising anti-AB antibodies reduce or prevent amyloid déposits. (p.12)

[…] the situation in the present case is different since […] the patent in suit itself already discloses experimental evidence that antibodies binding to [….] are not suitable for the claimed therapeutic application. Under these circumstances, no additional experimental evidence from the respondents is required, as they can rely on the evidence provided by the patent itself. This shifts the burden of proof back to the appellant, whose arguments must therefore fail. » (p. 16-17)

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Suffisance de description : non

- **T0760/12**

Rev 6 : Use of a substance that inhibits specific binding of HGF ß chain to c-Met in the preparation of a medicament for treating a pathological condition associated with activation of c-Met in a subject, wherein the substance is :

(a) a peptide comprising an amino acid sequence having at least 60 % sequence identity with the sequence VDWVCFRDLGCDWEL,

(b) a monoclonal antibody or a fragment thereof which specifically binds to said activated HGF ß chain; or

(c) a combination thereof, wherein the substance binds to activated HGF ß chain and inhibits specific binding of said activated HGF ß chain to c-met, and wherein the pathological condition is a tumor or angiogenesis-related disorder.

«The patent however does not disclose with the claimed specificity and function.[…] it has to be decided wether the provision of such an antibody and its potential suitability to exert the claimed therapeutic effect are both enabled in the patent…» (p. 9)

It thus next has to be examined wether it is made plausible in the patent that monoclonal antibodies as defined in the claim are potentially suitable for exerting a therapeutic effect….. »(p.10)

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Brevet EP délivré - Pas d'opposition

- EP 2933268 – The Board of Regents,
  The University of Texas system

1.Anticorps isolé, ou une partie de celui-ci liant l'antigène, qui se lie à OX40 humain comprenant : (a) une région variable CDR1 de chaine lourde comprenant la séquence……; (b) une région variable CDR2 de chaine lourde comprenant la séquence…..; (c) une région variable CDR3 de chaine lourde comprenant la séquence…; (d) une région variable CDR1 de chaine légère comprenant la séquence…; (e) une région variable CDR2 de chaine légère comprenant la séquence….;(f) une région variable CDR3 de chaine légère comprenant la séquence….

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Brevet EP délivré - Pas d'opposition

- EP 2926830 – Theraclone Sciences, The Scripps Research Institute, International Aids Vaccine initiative

1.Anti-corps anti-VIH monoclocal comprenant:

une séquence de chaîne lourde comprenant la séquence d'acides aminés de la SEQ ID NO:79 et une séquence de chaîne légère comprenant la séquence d'acides aminés de la SEQ ID NO: 149.

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Brevet EP délivré - Pas d'opposition

- EP 2857418 – University of Massachusetts, E.R. Squibs & Sons LLC

1.Anticorps humain monoclonal, ou partie de celui-ci se liant un antigène, qui se lie spécifiquement à la toxine B de *Clostridium difficile (C.difficile)*, dans lequel l'anticorps ou sa partie se liant à un antigène comprend une région de chaîne lourde variable comprenant la séquence d'acides aminés présentée dans la SEQ ID N0:54 et une région de chaîne légère variable comprenant la séquence d'acides aminés présentée dans la SEQ ID NO:58.

4. Composition pharmaceutique comprenant un anticorps, ou partie de celui-ci se liant à un antigène, qui se lie spécifiquement à la toxine B de *C.difficile* avec une valeur KD inférieure à 10 $X10^{-10}$ M telle que mesurée par résonance plasmonique de surface et neutralise la toxine B de *C. difficile*, dans laquelle l'anticorps comprend :

(a)une région de chaîne lourde variable…. CDR1, CDR2 et CDR3…

(b) une région de chaîne légère variable…. CDR1, CDR2 et CDR3…

formulée pour une administration parentérale.

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Brevet EP délivré - Pas d'opposition

- EP 2853272 – Abbvie Biotherapeutics Inc.

1.Anticorps monoclonal antagoniste anti-CS1 ou fragment de liaison à un antigène antagoniste anti-CS1, de préférence humanisé, qui se lie à une protéine codée par SEQ ID NO:1, destiné à être utilisé dans le traitement du myélome chez un patient qui n'a pas développé de manifestations cliniques du myélome.

2.Anticorps ou fragment de liaison à un antigène destiné à être utilisé dans le traitement du myélome selon la revendication 1, qui inhibe la sécrétion d'immunoglobulines.

3. Anticorps ou fragment de liaison à un antigène destiné à être utilisé dans le traitement du myélome selon la revendication 1 ou la revendication 2, qui induit une cytotoxicité cellulaire dépendante des anticorps (« ADCC ») de cellules exprimant ladite protéine codée par SEQ ID N0:1.

4. Anticorps ou fragment de liaison à un antigène destiné à être utilisé dans le traitement du myélome selon l'une quelconque des revendications 1 à 3, qui induit au moins 40% de cytotoxicité, de préférence au moins 60% de cytotoxicité, de cellules exprimant ladite protéine codée par SEQ ID N0:1

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Brevet EP délivré - Pas d'opposition

- EP 2984108 – Lykera Biomed SA

1.Anticorps qui se lie spécifiquement à la protéine S100A7 ou fragment de celui-ci ayant la capacité de se lier audit antigène, pour son utilisation dans la prévention et/ou le traitement d'une maladie choisie parmi le cancer, une maladie associée à une angiogenèse indésirable, et une maladie associée à l'inflammation.

3. Anticorps pour son utilisation selon les revendications 1 ou 2 dans lequel la tumeur est caractérisée par une activation accrue de la voie MAPK et/ou une expression accrue du TNF-alpha.

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Brevet EP délivré - Pas d'opposition

- EP 2922875 – Sanofi

1.Anticorps isolé qui :

a) se lie au domaine A3-B3 des protéines CEACAM5 humaine et de *Macaca fascicularis*; et

b) ne présente pas de réaction croisée significative avec CEACAM1 humain, CEACAM6 humain, CEACAM7 humain, CEACAM8 humain, CEACAM1 de *Macaca fascicularis*, CEACAM6 de *Macaca fascicularis* et CEACAM8 de Macaca *fascicularis*.

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Brevet EP délivré - Pas d'opposition

- EP 2897978 – Abbvie Biotherapeutics Inc.

1. Variant d'un anticorps anti-TNFα de référence ou d'un fragment liant anti-TNFα de référence d'un anticorps, lequel anticorps ou fragment liant de référence comprend six CDR (régions déterminant la complémentarité) qui présentent les séquences d'acides aminés correspondant aux Séquences N° 5 (CDR-H1), N°6 (CDR-H2), N°7 (CDR-H3), N°8 (CDR-L1), N°9 (CDR-L2) et N°10 (CDR-L3), et lequel variant porte une substitution Y2K sur la région CDR-H1, et dans lequel les six CDR portent en tout jusqu'à 8 substitutions d'acide aminé, par rapport aux séquences des CDR de l'anticorps ou fragment liant de référence.

Merci pour votre attention

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Merci pour votre attention

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