Unexplained Abuses of Human IgG Subclass Denomination in Antibody Patents

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Patents possibly do (or do not) constitute a source of outstanding information for immunologists. For example, the use of pepsin to digest serum proteins without altering the antitoxin activity of antibodies was a breakthrough discovery by Ivan A. Parfentjev, only described in two patents (US2065196; US2123198) in the 1930s.

A recent patent database survey led us to identify 23 patent families (Table 1) filed on behalf of biopharmaceutical companies in the years 2008–2012, mentioning in their claims or in a particular embodiment of the specification the possibility of “creating chimaeric antibodies with human Fc regions derived from human IgG1, IgG2, IgG3, IgG4, IgG5, IgG6, IgG7, IgG8, IgG9, IgG10, IgG11, IgG12, IgG13, IgG14, IgG15, IgG16, IgG17, IgG18 or IgG19”. Where do these 15 new IgGs (IgG5 to IgG19) come from? Do they derive from newly described segmental duplications in the *IGH* locus on chromosome 14? Humans would then become the species with the largest number of IgG-encoding genes, outperforming horses, which have only seven IgG subclasses [1]. This bewildering numbering

could also result from confusion of IgG subclasses with the IgG allotype numerical system. This hypothesis is, however, unlikely, since IgG allotype numbering is discontinuous, goes far beyond 19, and requires at least one “m” character between G and the number (Gm1 to Gm28) [2, 3].

Despite these patents now dating back several years, there are absolutely no published peer-reviewed data describing more than four IgG subclasses in humans, despite the immunoglobulin heavy constant (IGHC) gene copy number variations observed in healthy individuals with multigene duplications [4, 5]. It is really surprising to see that pending or granted patents refer to IgG subclasses arising from boundless imagination, with the likely goal of freely overextending commercial exclusivity. Why stop at 19 subclasses when one could claim 29 or many more? We do not know whether patent attorneys are now more astute, are now more visionary, or err on the side of caution; however, what is certain is that Köhler and Milstein’s institution lacked foresight when it decided not to protect their hybridoma technology.

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Table 1 The 23 patents families where the abuses have been found

Patent family no.	Title	URL
WO2008144757	Novel rabbit antibody humanization methods and humanized rabbit antibodies	http://patentscope.wipo.int/search/en/WO2008144757
WO2008144763	Antibodies to IL-6 and use thereof	http://patentscope.wipo.int/search/en/WO2008144763
WO2008144753	Antibodies to TNF alpha and use thereof	http://patentscope.wipo.int/search/en/WO2008144753
US2009104187	Novel rabbit antibody humanization methods and humanized rabbit antibodies	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20090104187.PGNR
US2009238825	Novel rabbit antibody humanization methods and humanized rabbit antibodies	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20090238825.PGNR
US2009297513	Antibodies to IL-6 and use thereof	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20090297513.PGNR
US2009297436	Antibodies to IL-6 and use thereof	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20090297436.PGNR
US2010129357	Antibodies to IL-6 and use thereof	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20100129357.PGNR
WO2010065079	Antagonists of IL-6 to prevent or treat cachexia, weakness, fatigue and/or fever	http://patentscope.wipo.int/search/en/WO2010065079
US2010150829	Antibodies to IL-6 and use thereof	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20100150829.PGNR
WO2011066378	Antagonists of IL-6 to prevent or treat thrombosis	https://register.epo.org/application?number=EP10833914
US2011217303	Antagonists of IL-6 to prevent or treat cachexia, weakness, fatigue, and/or fever	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20110217303.PGNR
WO2011150454	Antibodies directed to the unprocessed receptor tyrosine kinase c-met	http://worldwide.espacenet.com/publicationDetails/biblio?CC=EP&NR=2576622A1&KC=A1&FT=D
US2012121594	Anti-IL-6 antibodies for the treatment of arthritis	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20120121594.PGNR
US2012128626	Anti-IL-6 antibodies for the treatment of anemia	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20120128626.PGNR
WO2012075340	Anti-NGF compositions and use thereof	http://patentscope.wipo.int/search/en/WO2012075340
US2012294797	Anti-CGRP compositions and use thereof	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20120294797.PGNR
US2012294802	Use of anti-CGRP antibodies and antibody fragments to prevent or inhibit photophobia or light aversion in subjects in need thereof, especially migraine sufferers	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20120294802.PGNR
US2012294822	Use of anti-CGRP or anti-CGRP-r antibodies or antibody fragments to treat or prevent chronic and acute forms of diarrhea	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20120294822.PGNR
WO2012161956	High-purity production of multi-subunit proteins such as antibodies in transformed microbes such as <i>Pichia pastoris</i>	http://patentscope.wipo.int/search/en/WO2012161956
US2013045888	Multi-copy strategy for high-titer and high-purity production of multi-subunit proteins such as antibodies in transformed microbes such as <i>Pichia pastoris</i>	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20130045888.PGNR
US2013058949	Antagonists of IL-6 to prevent or treat thrombosis	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20130058949.PGNR
US2013101598	Antagonists of IL-6 to prevent or treat thrombosis	http://appf1.uspto.gov/netaagi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PG01&p=1&u=/netahtml/PTO/srchnum.html&r=1&f=G&l=50&s1=20130101598.PGNR

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