Immune Checkpoint Antibodies

To meet your needs in the development and study of therapeutic monoclonal antibodies (mAbs) against immune checkpoints (ICs), InvivoGen offers a series of clinically relevant mAbs targeting CTLA-4, PD-1 or PD-L1, either in their original format, or with different/engineered isotypes conferring altered effector functions.

- Anti-hCTLA4 Isotype Family
- Anti-hPD1 Isotype Family
- Anti-hPD-L1 Isotype Family

InvivoGen's IC mAbs feature the Fab (fragment antigen binding) region of approved immune checkpoint inhibitors (ICIs; see table) and the Fc (crystallizable fragment) region of different immunoglobulin isotypes (see below), including the original. ICIs induce variable effector functions: ADCC (antibody dependent cellular cytotoxicity), ADCP (antibody dependent cellular phagocytosis), and CDC (complement dependent cytotoxicity). Depending on the necessity to protect or kill the target cells, ICIs' functions can be modulated through modification of the Fc region.

InvivoGen's IC antibodies are fully human mAbs. They are generated by recombinant DNA technology and produced in CHO cells. Their sequence, isotype, and binding activity are thoroughly verified.

InvivoGen ICI isotypes

	Native isotypes			Engineered isotypes		
	IgG1	IgG2	IgA2	IgG1NQ	IgG1fut	IgG4 (S228P)
ADCC	++	+/-	+/-	-	++++	+/-
ADCP	+++	+/-	+	-	+++	+
CDC	++	+	-	+/-	++	-

Potent effector function-inducing isotypes

IgG1 is the isotype of the majority of approved mAb therapies (e.g. anti-CTLA4 ipilimumab and anti-CD20 rituximab). It induces potent ADCC, ADCP and CDC, and thus can engage both humoral and cellular components of the immune system. IgG1-induced ADCC can be increased by defucosylation of the glycan sequences (**IgG1fut**). This modification, obtained by using a specific CHO cell line, enhances the mAb binding to FcγRIIIa/CD16. The approved anti-CD20 obinutuzumab is an engineered mAb with reduced fucose content. Also, a non-fucosylated variant of ipilimumab is currently under clinical trials.

Reduced effector function-inducing isotypes

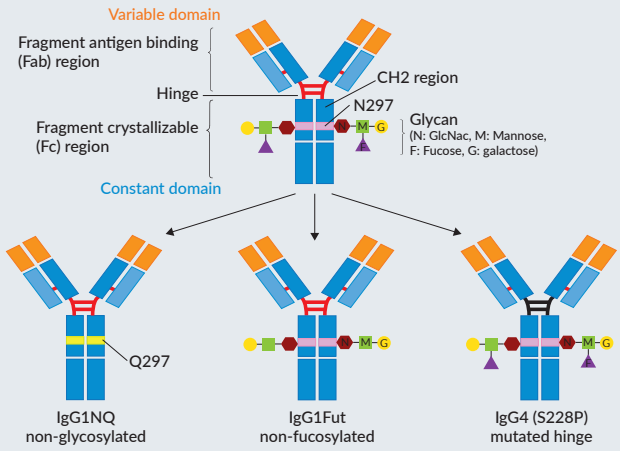
IgG1NQ and IgG1 (N298A) are engineered isotypes with a mutation in glycosylation sites of the CH2 domain, at position 297 (Asparagine (N) to Glutamine (Q)), and 298 ((Asparagine (N) to Alanine (A)), respectively. These non-glycosylated mAbs, such as the anti-PD-L1 atezolizumab, mostly act as blocking agents. They induce no ADCC nor ADCP, and only minimal CDC.

IgG2 induces poor ADCC and ADCP, while retaining some CDC function. Tremelimumab is an IgG2 targeting CTLA4 under clinical trials.

IgG4 (S228P) is an IgG4 engineered isotype that displays reduced ADCC, ADCP and no CDC. A Serine to Proline substitution at position 228 (S228P) in the hinge region prevents Fab arm exchanges frequently occuring between IgG4 molecules. IgG4 (S228P) mAbs, such as the anti-PD-1 nivolumab and pembrolizumab, mostly act as blocking agents.

IgA2 is a native isotype inducing low ADCC and ADCP, and no CDC. Although not yet introduced in clinal trials, IgAs have shown promising results in pre-clinical studies.

Examples of Strategies to Modify IgG mAb Isotypes



PRODUCT	CAT. CODE
Anti-hCTLA4 antibodies, variable regions of ipilimumab	
Anti-hCTLA4-hIgG1	hctla4-mab1
Anti-hCTLA4-hIgG1NQ	hctla4-mab12
Anti-hCTLA4-hIgG1fut	hctla4-mab13
Anti-hCTLA4-hIgG2	hctla4-mab2
Anti-hCTLA4-hIgG4 (S228P)	hctla4-mab14
Anti-hCTLA4-hIgA2	hctla4-mab7
Anti-hPD1 antibodies, variable regions of nivolumab	
Anti-hPD1-Ni-hIgG1	hpd1ni-mab1
Anti-hPD1-Ni-hIgG1NQ	hpd1ni-mab12
Anti-hPD1-Ni-hIgG1fut	hpd1ni-mab13
Anti-hPD1-Ni-hIgG2	hpd1ni-mab2
Anti-hPD1-Ni-hIgG4 (S228P)	hpd1ni-mab114
Anti-hPD1-Ni-hIgA2	hpd1ni-mab7
Anti-hPD1 antibodies, variable regions of pembrolizumab	
Anti-hPD1-Pem-hIgG1	hpd1pe-mab1
Anti-hPD1-Pem-hIgG1NQ	hpd1pe-mab12
Anti-hPD1-Pem-hIgG2	hpd1pe-mab2
Anti-hPD1-Pem-hIgG4 (S228P)	hpd1pe-mab14
Anti-hPD1-Pem-hIgA2	hpd1pe-mab7
Anti-hPD-L1 antibodies, variable regions of atezolizumab	
Anti-hPD-L1-hIgG1	hpdl1-mab1
Anti-hPD-L1-hIgG1 (N298A)	hpdl1-mab12
Anti-hPD-L1-hIgG1fut	hpdl1-mab13
Anti-hPD-L1-hIgG2	hpdl1-mab2

All antibodies are provided as 100 µg units. Larger quantities are available upon request.

Please visit our website for a full list of InvivoGen's engineered antibody isotype families.

www.invivogen.com/antibody-isotypes