29:2344-2353 and WO 99/56755. See also WO 99/61056; WO 00/06588; WO 00/16804; WO 00/21556; WO 00/54803; WO 00/61151; WO 00/67023; WO 00/67787 and U.S. Patent No. 6,090,791. See also Manzel et al. (1999) *Antisense Nucl. Acid Drug Dev.* 9:459-464; Verthelyi et al. (2001) J. Immunol. 166:2372-2377; WO 01/15726; WO 01/12223; WO 01/22972; WO 01/22990; WO 01/35991; WO 01/51500; WO 01/54720; U.S. Patent Nos. 6,174,872, 6,194,388, 6,207,646, 6,214,806, 6,218,371, 6,239,116. See also, WO 01/12804; WO 01/45750 ; WO 01/55341; WO 01/55370; WO 01/62207; WO 01/68077; WO 01/68078; WO 01/68103; WO 01/68116; WO 01/68117; WO 01/68143; WO 01/68144; WO 01/72123; WO 01/76642; WO 01/83503; WO 01/93902; WO 02/026757; WO 02/052002; WO 02/069369; WO 02/074922; U.S. Patent Nos. 6,339,068, 6,406,705, 6,426,334, 6,426,336, 6,429,199, 6,476,000.

[0010] Immunomodulatory polynucleotides generally include a CG sequence. Nucleotides flanking the CG of an IMP also appear to play a role in the immunomodulatory activity of the polynucleotide. There remains a need for continued identification of immunomodulatory polynucleotides.

[0011] All patents, patent applications, and publications cited herein are hereby incorporated by reference in their entirety.

DISCLOSURE OF THE INVENTION

[0012] The invention relates to immunomodulatory polynucleotides (IMP) and methods for modulating immune responses in individuals using these polynucleotides, particularly humans.

[0013] In one aspect, the invention provides immunomodulatory polynucleotides. In certain embodiments, the invention includes compositions which comprise any of the immunomodulatory polynucleotides described herein. The compositions may also include, for example, a pharmaceutically acceptable excipient or any of a number of other components, such as an antigen.

[0014] In one aspect, the immunomodulatory polynucleotide of the invention comprises (a) a palindromic sequence comprising at least two CG dinucleotides, wherein the CG dinucleotides are separated by 0, 1, 2, 3, 4 or 5 bases and wherein the palindromic sequence is at least 8 bases in length; and (b) a $(TCG)_y$ sequence, wherein y is 1, wherein the 5' T of the $(TCG)_y$ sequence is positioned 0 bases from the 5' end of the

polynucleotide; wherein the palindromic sequence of (a) includes all or part of the $(TCG)_y$ sequence; and wherein a CG of the $(TCG)_y$ sequence may be one of the CG dinucleotides of the palindromic sequence of (a), wherein the polynucleotide is 15-50 bases or base pairs in length. In some immunomodulatory polynucleotides of the invention, whether described in this paragraph or elsewhere in this application, the palindromic sequence has a base composition of more than one-third A's and T's.

[0015] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2CGX_2'X_1')_z$ (SEQ ID NO:156), wherein N are nucleosides, x = 0, y = 1, w = 0, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, and wherein the 5'T of the $(TCG(N_q))_y$ sequence is 0 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first $(X_1X_2CGX_2'X_1')$ of the $(X_1X_2CGX_2'X_1'(CG)_p)_z$ sequences. In some embodiments, the IMP comprises a sequence selected from the group consisting of SEQ ID NO:39, SEQ ID NO:117, SEQ ID NO:171, SEQ ID NO:175, and SEQ ID NO:172.

[0016] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2CGX_3X_3'CGX_2'X_1'(CG)_p)_z$ (SEQ ID NO:159), wherein N are nucleosides, x = 0, y = 1, w = -2, -1, 0, 1 or 2, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and $X_2'$are self-complimentary nucleosides, X_3 and X_3' are self-complimentary nucleosides and wherein the 5'T of the $(TCG(N_q))_y$ sequence is 0 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 10 bases in length wherein the palindromic sequence comprises the first $(X_1X_2CGX_3X_3'CGX_2'X_1')$ of the $(X_1X_2CGX_3X_3'CGX_2'X_1'(CG)_p)_z$ sequences.

[0017] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2X_3X_4X_5CGX_5'X_4'X_3'X_2'X_1'(CG)_p)_z$ (SEQ ID NO:160), wherein N are nucleosides, x = 0, y = 1, w = -3, -2, -1, 0, 1 or 2, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, X_3 and X_3' are self-complimentary nucleosides, X_4 and X_4' are self-complimentary nucleosides, X_5 and X_5' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0 bases from the 5'

end of the polynucleotide; and (b) a palindromic sequence at least 12 bases in length wherein the palindromic sequence comprises the first ($X_1X_2X_3X_4X_5CGX_5'X_4'X_3'X_2'X_1'$) of the ($X_1X_2X_3X_4X_5CG\ X_5'X_4'X_3'X_2'X_1'(CG)_p)_z$ sequences.

[0018] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(CGX_1X_1'CG(CG)_p)_z$ (SEQ ID NO: 161), wherein N are nucleosides, x = 0, y = 1, w = -2, 0, 1 or 2, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, wherein X_1 and X_1' are self-complimentary nucleosides and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first ($CGX_1X_1'CG$) of the ($CG\ X_1X_1'CG\ (CG)_p)_z$ sequences.

[0019] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1CGCGX_1'(CG)_p)_z$ (SEQ ID NO: 162), wherein N are nucleosides, x = 0, y = 1, w = -1, 0, 1 or 2, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first (X_1CGCGX_1') of the $(X_1CGCGX_1'(CG)_p)_z$ sequences.

[0020] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2CGCGX_2'X_1'(CG)_p)_z$ (SEQ ID NO: 163), wherein N are nucleosides, x = 0, y = 1, w = -2, -1, 0, 1 or 2, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first ($X_1X_2CGCG\ X_2'X_1'$) of the ($X_1X_2CGCG\ X_2'X_1'(CG)_p)_z$ sequences.

[0021] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2X_3CGCGX_3'\ X_2'X_1'(CG)_p)_z$ (SEQ ID NO: 164), wherein N are nucleosides, x = 0, y = 1, w = -3, -2, -1, 0,1 or 2, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, X_3 and X_3' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0 bases from the 5' end of the

polynucleotide; and (b) a palindromic sequence at least 10 bases in length wherein the palindromic sequence comprises the first ($X_1X_2X_3CGCGX_3'$ $X_2'X_1'$) of the ($X_1X_2X_3CGCGX_3'$ $X_2'X_1'(CG)_p)_z$ sequences.

[0022] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(CGX_1X_2X_2'X_1'CG(CG)_p)_z$ (SEQ ID NO: 165), wherein N are nucleosides, x = 0, y = 1, w = -2, 0, 1 or 2, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first ($CGX_1X_2X_2'X_1'CG$) of the ($CGX_1X_2X_2'X_1'CG(CG)_p)_z$ sequences.

[0023] In another aspect, the immunomodulatory polynucleotide of the invention comprises a modification of one or more phosphate groups and wherein the modification of one of more phosphate groups is a phosphorothioate linkage.

[0024] In another aspect, the invention provides use of the immunomodulatory polynucleotide of the invention in the manufacture of a medicament to modulate an immune response in an individual. Immunomodulation according to the uses of the invention may be practiced on individuals including those suffering from a disorder associated with a Th2-type immune response (*e.g.*, allergies, allergy-induced asthma, or atopic dermatitis), individuals receiving vaccines such as therapeutic vaccines (*e.g.*, vaccines comprising an allergy epitope, a mycobacterial epitope, or a tumor associated epitope) or prophylactic vaccines, individuals with cancer and individuals having an infectious disease.

[0025] In another aspect, the invention provides use of the immunomodulatory polynucleotide of the invention in the manufacture of a medicament to increase interferon-gamma (IFN-γ) in an individual. Administration of an immunomodulatory polynucleotide in accordance with the invention increases IFN-γ in the individual.

[0026] In another aspect, the invention provides use of the immunomodulatory polynucleotide of the invention in the manufacture of a medicament to ameliorate a symptom of an infectious disease in an individual. Administration of an immunomodulatory polynucleotide in accordance with the invention ameliorates one or more symptoms of the infectious disease.

[0027] In another aspect, the invention provides use of the immunomodulatory polynucleotide of the invention in the manufacture of a medicament to ameliorate a symptom of an IgE-related disorder in an individual. Administration of an immunomodulatory polynucleotide in accordance with the invention ameliorates one or more symptoms of the IgE-related disorder.

[0028] In another aspect, the invention provides use of the immunomodulatory polynucleotide of the invention in the manufacture of a medicament to treat asthma.

[0029] The invention further relates to kits, preferably for carrying out the methods of the invention. The kits of the invention generally comprise an immunomodulatory polynucleotide of the invention (generally in a suitable container), and may further include instructions for use of the immunomodulatory polynucleotide in immunomodulation of an individual.

BRIEF DESCRIPTION OF THE DRAWINGS

[0030] Fig. 1 is a graph depicting the amount of IFN-α, produced (pg/ml) from human PBMCs in response to varying doses of four different IMPs: SEQ ID NOs: 1, 27, 113 and 172.

[0031] Fig. 2 contains graphs depicting NK cell lytic activity stimulated by IMPs.

MODES FOR CARRYING OUT THE INVENTION

[0032] We have discovered immunomodulatory polynucleotides and methods for modulating immune responses in individuals, particularly humans, using these immunomodulatory polynucleotides. The compositions of the invention comprise an immunomodulatory polynucleotide as described herein. The immunomodulatory polynucleotides of the invention include a) a palindromic sequence at least 8 bases in length which contains at least one CG dinucleotide and b) at least one TCG trinucleotide at or near the 5' end of the polynucleotide.

[0033] We have found that immunomodulatory polynucleotides of the invention efficiently modulate immune cells, including human cells, in a variety of ways. We have observed that immunomodulatory polynucleotides of the invention can effectively stimulate cytokine,

29:2344-2353 and WO 99/56755. See also WO 99/61056; WO 00/06588; WO 00/16804; WO 00/21556; WO 00/54803; WO 00/61151; WO 00/67023; WO 00/67787 and U.S. Patent No. 6,090,791. See also Manzel et al. (1999) *Antisense Nucl. Acid Drug Dev.* 9:459-464; Verthelyi et al. (2001) *J. Immunol.* 166:2372-2377; WO 01/15726; WO 01/12223; WO 01/22972; WO 01/22990; WO 01/35991; WO 01/51500; WO 01/54720; U.S. Patent Nos. 6,174,872, 6,194,388, 6,207,646, 6,214,806, 6,218,371, 6,239,116. See also, WO 01/12804; WO 01/45750; WO 01/55341; WO 01/55370; WO 01/62207; WO 01/68077; WO 01/68078; WO 01/68103; WO 01/68116; WO 01/68117; WO 01/68143; WO 01/68144; WO 01/72123; WO 01/76642; WO 01/83503; WO 01/93902; WO 02/026757; WO 02/052002; WO 02/069369; WO 02/074922; U.S. Patent Nos. 6,339,068, 6,406,705, 6,426,334, 6,426,336, 6,429,199, 6,476,000.

[0010] Immunomodulatory polynucleotides generally include a CG sequence. Nucleotides flanking the CG of an IMP also appear to play a role in the immunomodulatory activity of the polynucleotide. There remains a need for continued identification of immunomodulatory polynucleotides.

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[0012] The invention relates to immunomodulatory polynucleotides (IMP) and methods for modulating immune responses in individuals using these polynucleotides, particularly humans.

[0013] In one aspect, the invention provides immunomodulatory polynucleotides. In certain embodiments, the invention includes compositions which comprise any of the immunomodulatory polynucleotides described herein. The compositions may also include, for example, a pharmaceutically acceptable excipient or any of a number of other components, such as an antigen.

[0014] In one aspect, the immunomodulatory polynucleotide of the invention comprises (a) a palindromic sequence comprising at least two CG dinucleotides, wherein the CG dinucleotides are separated by 0, 1, 2, 3, 4 or 5 bases and wherein the palindromic sequence is at least 8 bases in length; and (b) a $(TCG)_y$, wherein y is 1 or 2, wherein the 5' T of the $(TCG)_y$ is positioned 0, 1, 2 or 3 bases from the 5' end of the polynucleotide and wherein the $(TCG)_y$ is separated from the 5' end of the palindromic sequence by 0, 1, or 2 bases. In some immunomodulatory polynucleotides of the invention, whether described in this paragraph or

elsewhere in this application, the palindromic sequence has a base composition of less than two-thirds G's and C's. In some embodiments, the palindromic sequence has a base composition of greater than one-third A's and T's.

[0015] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) a palindromic sequence comprising at least two CG dinucleotides, wherein the CG dinucleotides are separated by 0, 1, 2, 3, 4 or 5 bases and wherein the palindromic sequence is at least 8 bases in length; and (b) a $(TCG)_y$ sequence, wherein y is 1 or 2, wherein the 5' T of the $(TCG)_y$ sequence is positioned 0, 1, 2 or 3 bases from the 5' end of the polynucleotide, and further wherein the palindromic sequence of (a) includes all or part of the $(TCG)_y$ sequence and wherein a CG of the $(TCG)_y$ sequence may be one of the CG dinucleotides of the palindromic sequence of (a).

[0016] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2CGX_2'X_1'(CG)_p)_z$ (SEQ ID NO: 156) wherein N are nucleosides, x = 0-3, y = 1-4, w = -2, -1, 0, 1 or 2, p= 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0-3 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first ($X_1X_2CGX_2'X_1'$) of the $(X_1X_2CGX_2'X_1'(CG)_p)_z$ sequences. In some embodiments, X_1 and X_2 are each either A or T.

[0017] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2CGX_3X_3'CGX_2'X_1'(CG)_p)_z$ (SEQ ID NO: 159) wherein N are nucleosides, x = 0-3, y = 1-4, w = -2, -1, 0, 1 or 2, p= 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, X_3 and X_3' are self-complimentary nucleosides and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0-3 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 10 bases in length wherein the palindromic sequence comprises the first ($X_1X_2CGX_3X_3'CGX_2'X_1'$) (SEQ ID NO:216) of the $(X_1X_2CGX_3X_3'CGX_2'X_1'(CG)_p)_z$ (SEQ ID NO:217) sequences. In some embodiments, when p=1, X_1, X_2, and X_3 are each either A or T. In some embodiments, when p=0, at least two of X_1, X_2, and X_3 are either A or T.

[0018] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2X_3X_4X_5CGX_5'X_4'X_3'X_2'X_1'(CG)_p)_z$ (SEQ ID NO:160) wherein N are nucleosides, x = 0-3, y = 1-4, w = -3, -2, -1, 0, 1 or 2, p= 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary

nucleosides, X_3 and X_3' are self-complimentary nucleosides, X_4 and X_4' are self-complimentary nucleosides, X_5 and X_5' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0-3 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 12 bases in length wherein the palindromic sequence comprises the first ($X_1X_2X_3X_4X_5CGX_5'X_4'X_3'X_2'X_1'$) (SEQ ID NO:218) of the $(X_1X_2X_3X_4X_5CGX_5'X_4'X_3'X_2'X_1'(CG)_p)_z$ (SEQ ID NO:219)sequences. In some embodiments, at least three of X_1, X_2, X_3, X_4, and X_5 are either A or T.

[0019] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(CGX_1X_1'CG(CG)_p)_z$ (SEQ ID NO:161) wherein N are nucleosides, x = 0-3, y = 1-4, w = -2, 0, 1 or 2, p= 0 or 1, q = 0, 1 or 2, and z = 1-20, wherein X_1 and X_1' are self-complimentary nucleosides and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0-3 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first ($CGX_1X_1'CG$) of the $(CGX_1X_1'CG(CG)_p)_z$ sequences.

[0020] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1CGCGX_1'(CG)_p)_z$ (SEQ ID NO:162) wherein N are nucleosides, x = 0-3, y = 1-4, w = -1, 0, 1 or 2, p = 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0-3 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first (X_1CGCGX_1') of the $(X_1CGCGX_1'(CG)_p)_z$ sequences.

[0021] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2CGCGX_2'X_1'(CG)_p)_z$ (SEQ ID NO:163) wherein N are nucleosides, x = 0-3, y = 1-4, w = -2, -1, 0, 1 or 2, p= 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0-3 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first ($X_1X_2CGCGX_2'X_1'$) of the $(X_1X_2CGCGX_2'X_1'(CG)_p)_z$ (SEQ ID NO:220) sequences. In some embodiments, X_1 and X_2 are each either A or T.

[0022] In another aspect, the immunomodulatory polynucleotide of the invention comprises (a) 5'-$N_x(TCG(N_q))_yN_w(X_1X_2X_3CGCGX_3'X_2'X_1'(CG)_p)_z$ (SEQ ID NO:164) wherein N are nucleosides, x = 0-3, y = 1-4, w = -3, -2, -1, 0, 1 or 2, p= 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1

and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, X_3 and X_3' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0-3 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 10 bases in length wherein the palindromic sequence comprises the first ($X_1X_2X_3CGCGX_3'X_2'X_1'$) (SEQ ID NO:221)of the $(X_1X_2X_3CGCGX_3'X_2'X_1'(CG)_p)_z$ (SEQ ID NO:222) sequences. In some embodiments, when p=1, X_1, X_2, and X_3 are each either A or T. In some embodiments, when p=0, at least two of X_1, X_2, and X_3 are either A or T.

[0023] In another aspect, the immunomodulatory polynucleotide of the invention comprises a) 5'-$N_x(TCG(N_q))_yN_w(CGX_1X_2X_2'X_1'CG(CG)_p)_z$ (SEQ ID NO:165) wherein N are nucleosides, x = 0-3, y = 1-4, w = -2, 0, 1 or 2, p= 0 or 1, q = 0, 1 or 2, and z = 1-20, X_1 and X_1' are self-complimentary nucleosides, X_2 and X_2' are self-complimentary nucleosides, and wherein the 5' T of the $(TCG(N_q))_y$ sequence is 0-3 bases from the 5' end of the polynucleotide; and (b) a palindromic sequence at least 8 bases in length wherein the palindromic sequence comprises the first ($CGX_1X_2X_2'X_1'CG$) of the $(CGX_1X_2X_2'X_1'CG(CG)_p)_z$ (SEQ ID NO:223) sequences. In some embodiments, X_1 and X_2 are each either A or T.

[0024] In another aspect, the invention provides methods of modulating an immune response in an individual, comprising administering to an individual an immunomodulatory polynucleotide of the invention in an amount sufficient to modulate an immune response in said individual. Immunomodulation according to the methods of the invention may be practiced on individuals including those suffering from a disorder associated with a Th2-type immune response (*e.g.*, allergies, allergy-induced asthma, or atopic dermatitis), individuals receiving vaccines such as therapeutic vaccines (*e.g.*, vaccines comprising an allergy epitope, a mycobacterial epitope, or a tumor associated epitope) or prophylactic vaccines, individuals with cancer and individuals having an infectious disease.

[0025] In another aspect, the invention provides methods of increasing interferon-gamma (IFN-γ) in an individual, comprising administering an effective amount of an immunomodulatory polynucleotide of the invention to said individual. Administration of an immunomodulatory polynucleotide in accordance with the invention increases IFN-γ in the individual.

[0026] In another aspect, the invention provides methods of increasing interferon-alpha (IFN-α) in an individual, comprising administering an effective amount of an immunomodulatory polynucleotide of the invention to said individual. Administration of an

immunomodulatory polynucleotide in accordance with the invention increases IFN-α in the individual.

[0027] In another aspect, the invention provides methods of ameliorating one or more symptoms of an infectious disease, comprising administering an effective amount of an immunomodulatory polynucleotide of the invention to an individual having an infectious disease. Administration of an immunomodulatory polynucleotide in accordance with the invention ameliorates one or more symptoms of the infectious disease.

[0028] In another aspect, the invention provides methods of ameliorating one or more symptoms of an IgE-related disorder, comprising administering an effective amount of an immunomodulatory polynucleotide of the invention to an individual having an IgE-related disorder. Administration of an immunomodulatory polynucleotide in accordance with the invention ameliorates one or more symptoms of the IgE-related disorder.

[0029] The invention further relates to kits, preferably for carrying out the methods of the invention. The kits of the invention generally comprise an immunomodulatory polynucleotide of the invention (generally in a suitable container), and may further include instructions for use of the immunomodulatory polynucleotide in immunomodulation of an individual.

BRIEF DESCRIPTION OF THE DRAWINGS

[0030] Fig. 1 is a graph depicting the amount of IFN-α produced (pg/ml) from human PBMCs in response to varying doses of four different IMPs: SEQ ID NOs: 1, 27, 113 and 172.

[0031] Fig. 2 contains graphs depicting NK cell lytic activity stimulated by IMPs.

MODES FOR CARRYING OUT THE INVENTION

[0032] We have discovered immunomodulatory polynucleotides and methods for modulating immune responses in individuals, particularly humans, using these immunomodulatory polynucleotides. The compositions of the invention comprise an immunomodulatory polynucleotide as described herein. The immunomodulatory polynucleotides of the invention include a) a palindromic sequence at least 8 bases in length which contains at least one CG dinucleotide and b) at least one TCG trinucleotide at or near the 5' end of the polynucleotide.

[0033] We have found that immunomodulatory polynucleotides of the invention efficiently modulate immune cells, including human cells, in a variety of ways. We have observed that immunomodulatory polynucleotides of the invention can effectively stimulate cytokine,