CLAIMS

What is claimed is:

1. A C-type lectin domain family 9 member A (Clec9A) binding agent comprising an amino acid sequence having at least 95% identity with SEQ ID NO: 332, wherein the Clec9A binding agent comprises three complementarity determining regions (CDR1, CDR2, and CDR3), wherein:

(a) CDR1 comprises an amino acid sequence of SEQ ID NO: 51 or 56;

(b) CDR2 comprises an amino acid sequence of SEQ ID NO: 136 or 191; and

(c) CDR3 comprises an amino acid sequence of SEQ ID NO: 202.

2. The Clec9A binding agent of claim 1, wherein the amino acid sequence is selected from SEQ ID NOs: 333-336.

3. The Clec9A binding agent of any one of the above claims, wherein the Clec9A binding agent comprises one or more signaling agents.

4. The Clec9A binding agent of claim 3, wherein the signaling agent is selected from one or more of an interferon, an interleukin, and a tumor necrosis factor, any of which are optionally modified.

5. The Clec9A binding agent of any one of the above claims, wherein the Clec9A binding agent comprises one or more additional targeting moieties.

6. The Clec9A binding agent of claim 5, wherein the one or more additional targeting moieties recognize and optionally functionally modulate a tumor antigen.

7. The Clec9A binding agent of claim ~~6~~5, wherein the one or more additional targeting moieties recognize and optionally functionally modulate an antigen on an immune cell.

8. The Clec9A binding agent of claim 7, wherein the immune cell is selected from a T cell, a B cell, a dendritic cell, a macrophage, neutrophil, and a NK cell.

9. The Clec9A binding agent of any of the above claims, wherein the Clec9A binding agent recruits cytotoxic T cells to tumor cells or to the tumor environment.

10. The Clec9A binding agent of any of the above claims, wherein the Clec9A binding agent recognizes and binds Clec9A without functionally modulating its activity.

11. A recombinant nucleic acid composition encoding the Clec9A binding agents of any one of the above claims.

12. A host cell comprising a nucleic acid of claim 11.

13. Use of the Clec9A binding agent of claim 1 or 2 in the manufacture of a medicament for treating or preventing cancer.

14. The use of the Clec9A binding agent of claim 13, wherein the cancer is selected form one or more of basal cell carcinoma, biliary tract cancer; bladder cancer; bone cancer; brain and central nervous system cancer; breast cancer; cancer of the peritoneum; cervical cancer; choriocarcinoma; colon and rectum cancer; connective tissue cancer; cancer of the digestive system; endometrial cancer; esophageal cancer; eye cancer; cancer of the head and neck; gastric cancer (including gastrointestinal cancer); glioblastoma; hepatic carcinoma; hepatoma; intra-epithelial neoplasm; kidney or renal cancer; larynx cancer; leukemia; liver cancer; lung cancer (*e.g.*, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, and squamous carcinoma of the lung); melanoma; myeloma; neuroblastoma; oral cavity cancer (lip, tongue, mouth, and pharynx); ovarian cancer; pancreatic cancer; prostate cancer; retinoblastoma; rhabdomyosarcoma; rectal cancer; cancer of the respiratory system; salivary gland carcinoma; sarcoma; skin cancer; squamous cell cancer; stomach cancer; testicular cancer; thyroid cancer; uterine or endometrial cancer; cancer of the urinary system; vulval cancer; lymphoma including Hodgkin's and non-Hodgkin's lymphoma, as well as B-cell lymphoma (including low grade/follicular non-Hodgkin's lymphoma (NHL); small lymphocytic (SL) NHL; intermediate grade/follicular NHL; intermediate grade diffuse NHL; high grade immunoblastic NHL; high grade lymphoblastic NHL; high grade small non-cleaved cell NHL; bulky disease NHL; mantle cell lymphoma; AIDS-related lymphoma; and Waldenstrom's Macroglobulinemia; chronic lymphocytic leukemia (CLL); acute lymphoblastic leukemia (ALL); Hairy cell leukemia; chronic myeloblastic leukemia; as well as other carcinomas and sarcomas; and post-transplant lymphoproliferative disorder (PTLD), as well as abnormal vascular proliferation associated with phakomatoses, edema (*e.g.* that associated with brain tumors), and Meigs' syndrome.

15. Use of the Clec9A binding agent of claim 1 or 2 in the manufacture of a medicament for treating or preventing an autoimmune and/or neurodegenerative disease.

16. The use of the Clec9A binding of claim 15, wherein the autoimmune and/or neurodegenerative disease is selected from multiple sclerosis, diabetes mellitus, lupus, celiac disease, Crohn's disease, ulcerative colitis, Guillain-Barre syndrome, scleroderms, Goodpasture's syndrome, Wegener's granulomatosis, autoimmune epilepsy, Rasmussen's encephalitis, Primary biliary sclerosis, Sclerosing cholangitis, Autoimmune hepatitis, Addison's disease, Hashimoto's thyroiditis, Fibromyalgia, Menier's syndrome; transplantation rejection (*e.g.*, prevention of allograft rejection) pernicious anemia, rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, Sjogren's syndrome, lupus erythematosus, myasthenia gravis, Reiter's syndrome, Grave's disease.

17. The use of Clec9A binding agent of claim 16, wherein the autoimmune and/or neurodegenerative disease is multiple sclerosis.

~~18. The use of any one of claims 15-17, wherein the Clec9A binding agent leads to immunosuppression in the patient.~~

~~19~~13. A chimeric protein comprising:

(a) a Clec9A binding agent of any one of claims 1-10; and

(b) a modified human IFN-α2 comprising one or more mutations at positions R120, M148, R149, and L153, relative to SEQ ID NO: 337 or 338~~, said modified human IFN-α2 having one or more mutations that confer improved safety as compared to a wild type IFN-α2~~; and

wherein the Clec9A binding agent~~targeting moiety~~ and the modified human IFN-α2~~signaling agent~~ are optionally connected with one or more linkers.

~~20~~14. The chimeric protein of claim ~~19~~13, wherein the modified human IFN-α2 comprises one or more mutations selected from R120E, R149A, and L153A.

~~21~~15. The chimeric protein of claim ~~19~~13, wherein the modified human IFN-α2 comprises a R120E mutation and either a R149A or a L153A mutation.

~~22~~16. A chimeric protein comprising:

(a) a Clec9A binding agent of any one of claims 1-10; and

(b) a modified human IFN-β comprising one or more mutations at positions W22, R27, L32, R35, V148, L151, R152, and Y155, relative to SEQ ID NO: 339~~, said modified human IFN-β having one or more mutations that confer improved safety as compared to a wild type IFN-β~~; and

wherein the Clec9A binding agent~~targeting moiety~~ and the modified human IFN-β~~signaling agent~~ are optionally connected with one or more linkers.

~~23~~17. The chimeric protein of claim ~~22~~16, wherein the modified human IFN-β comprises one or more mutations selected from W22G, R27G, L32A, L32G, R35A, R35G, V148G, L151G, R152A, R152G.

~~24. Use of any one of the Clec9A binding agents of claims 1-10 or any one of the chimeric proteins of claims 19-23 in the manufacture of a medicament for treating one or more of: cancer, infections, immune disorders, and/or autoimmune diseases.~~

~~25. The Clec9A binding agent of claim 1 or claim 2, wherein the Clec9A binding agent comprises three complementarity determining regions (CDR1, CDR2, and CDR3), wherein:~~

~~(a) CDR1 comprises an amino acid sequence of SEQ ID NO: 51;~~

~~(b) CDR2 comprises an amino acid sequence of SEQ ID NO: 136; and~~

~~(c) CDR3 comprises an amino acid sequence of SEQ ID NO: 202.~~