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LIFE SCIENCES
insights

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Autoimmune Disease Biomarkers APRIL & BAFF

The B cell-stimulating molecules, BAFF (B cell activating factor also known as BLyS; TALL-1; CD257 or TNFSF13B) and APRIL (a proliferation-inducing ligand, also known as CD256 or TNFSF13), are critical factors in the maintenance of the B cell pool and humoral immunity. They are implicated in several human autoimmune diseases with autoreactive B cell involvement, including systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), IgA nephropathy (IgAN) and rheumatoid arthritis (RA). APRIL might also function in enhancing proliferation of some tumor cells, especially B cell malignancies and BAFF levels are increased in some lymphoid cancers.

Best-In-Class APRIL & BAFF ELISA Kits

UNIQUE

NEW APRIL (human) ELISA Kit
The BEST on the Market!

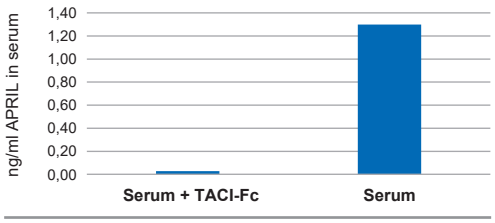
The APRIL (human) ELISA Kit (Prod. No. AG-45B-0012) is a sandwich ELISA for specific quantitative determination of human APRIL in serum, plasma and cell culture supernatants. This ELISA Kit shows both high specificity and high sensitivity, which is a clear advantage compared to other APRIL (human) ELISA Kits from key competitors.

NEW **APRIL (human) ELISA Kit**

AG-45B-0012 96 wells

Sensitivity: 7 pg/ml
Range: 7.8 to 500 pg/ml
Sample: Cell Culture Supernatant, Plasma, Serum

Specificity: Serum from a healthy patient is left untreated or treated with 1 µg/ml of the APRIL receptor, TACI (human):Fc (human) (Prod. No. AG-40B-0079). APRIL levels were measured using the APRIL (human) ELISA Kit (Prod. No. AG-45B-0012).



BAFF, Soluble (human) ELISA Kit (hypersensitive) *The RELIABLE Assay*

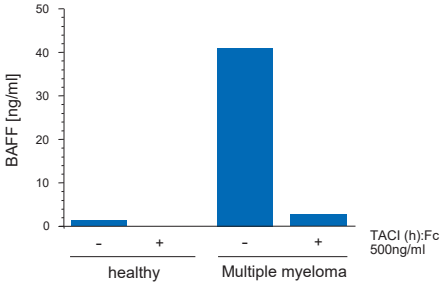
The BAFF, Soluble (human) ELISA Kit (Prod. No. AG-45B-0001) is a sandwich ELISA for specific quantitative determination of human BAFF in serum, plasma and cell culture supernatants. This ELISA Kit does not cross-react with mouse BAFF and has been chosen by several CROs for its high specificity and high sensitivity.

BAFF, Soluble (human) ELISA Kit (hypersensitive)

AG-45B-0001 96 wells

Sensitivity: 8 pg/ml
Range: 15.6 to 500 pg/ml
Sample: Cell Culture Supernatant, Plasma, Serum

Specificity: Serum from a healthy patient or patient with multiple sclerosis is left untreated or treated with 0.5 µg/ml of a BAFF receptor, TACI (human):Fc (human) (AG-40B-0079). BAFF levels are measured using the BAFF, Soluble (human) ELISA Kit (hypersensitive) (Prod. No. AG-45B-0001).



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Autoimmune Disease Biomarkers APRIL & BAFF

The B cell-stimulating molecules, BAFF (B cell activating factor also known as BLyS; TALL-1; CD257 or TNFSF13B) and APRIL (a proliferation-inducing ligand, also known as CD256 or TNFSF13), are critical factors in the maintenance of the B cell pool and humoral immunity (1, 2).

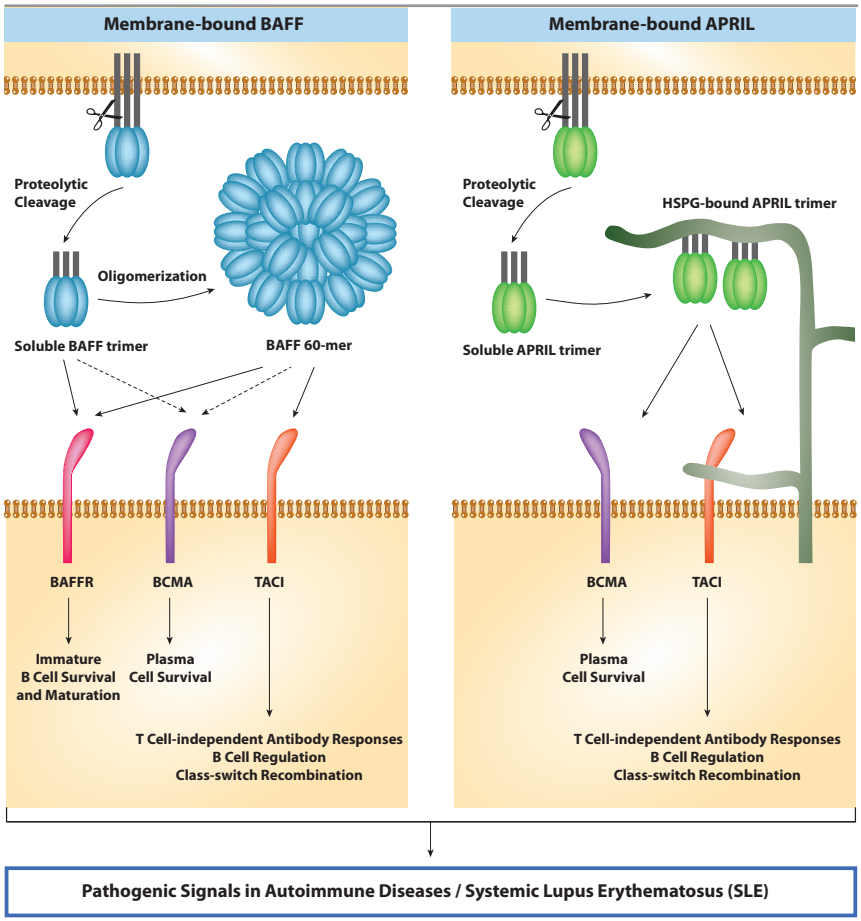
APRIL is a secreted protein that binds to transmembrane activator and CAML interactor (TACI), B cell maturation antigen (BCMA) and heparan sulfate proteoglycans (HSPG). APRIL can interact with carbohydrate side chains of proteoglycans that may trigger cross-linkng (3).

BAFF is a transmembrane protein which is proteolytically processed by furin to be released as a soluble cytokine (2). Soluble BAFF exists either as trimers (BAFF 3-mer), or as an ordered assembly of 20 trimers (BAFF 60-mer) (4). BAFF 3-mer and BAFF 60-mer both signal through BAFF-R, only TACI (and BCMA) respond to BAFF 60-mer and not to BAFF 3-mer (4). Similar observations are true with APRIL, which needs to be cross-linked in order to activate TACI (4).

APRIL maintains B cell homeostasis by acting at a later stage, modulating the function and survival of antigen-experienced B cells. BAFF is a key survival factor for peripheral B cells and together with IL-6 plasma cell differentiation (2). APRIL (as well as BAFF) stimulates class-switch recombination (CSR), hence contributes to shaping humoral effector mechanisms. With regards to humoral memory, APRIL is involved in the establishment and survival of the long-lived plasma cell (LLPC) pool in the bone marrow (BM) (5). Besides its major role in B cell biology, BAFF co-stimulates activated T cells. A recent study reports that APRIL confers atheroprotection by binding to heparan sulfate chains of heparan-sulfate proteoglycan 2 (HSPG2), which limits the retention of low-density lipoproteins, accumulation of macrophages and formation of necrotic cores (13).

APRIL is expressed by a number of myeloid-derived cell types including BM granulocytes, megakaryocytes, eosinophils, osteoclasts, and by dendritic cells following exposure to IFN-α, IFN-γ or CD40L. APRIL expression is induced during hematopoiesis in the bone marrow. APRIL expression is not limited to cells of myeloid origin but can be found in epithelial cells of the gut, tonsil, breast and skin. Finally, APRIL is expressed in tumor cell lines and human cancer cells of colon, thyroid and lymphoid origin (1). BAFF is mainly produced by innate immune cells such as neutrophils, monocytes, macrophages, dendritic cells, follicular dendritic cells, T cells, activated B cells, some malignant B cells, but non-lymphoid cells like astrocytes, synoviocytes and epithelial cells can also produce BAFF.

BAFF and APRIL are implicated in several human autoimmune diseases with autoreactive B cell involvement, including systemic lupus erythematosus (SLE) (6), Sjögren's syndrome (SS) (7), IgA nephropathy (IgAN) (8), and rheumatoid arthritis (RA) (9). APRIL might also function in enhancing proliferation of some tumor cells, especially B cell malignancies (10, 11). BAFF levels are also increased in some lymphoid cancers (12).



LITERATURE REFERENCES: [1] Targeting BAFF and APRIL in systemic lupus erythematosus and other antibody-associated diseases: E. Samy, et al.; Int. Rev. Immunol. **36,** 3 (2017) • **[2]** Cracking the BAFF code: F. Mackay & P. Schneider; Nat. Rev. Immunol. **9,** 491 (2009) • **[3]** Identification of proteoglycans as the APRIL-specific binding partners: K. Ingold, et al.; J. Exp. Med. **201,** 1375 (2005) • **[4]** TACI, unlike BAFF-R, is solely activated by oligomeric BAFF and APRIL to support survival of activated B cells and plasmablasts: C. Bossen, et al.; Blood **111,** 1004 (2009) • **[5]** Factors of the bone marrow microniche that support human plasma cell survival and immunoglobulin secretion: D.C. Nguyen, et al.; Nat. Commun. **12,** 3698 (2018) • **[6]** Raised serum APRIL levels in patients with systemic lupus erythematosus: T. Koyama, et al.; Ann. Rheum. Dis. **64,** 1065 (2005) • **[7]** The expression of APRIL in Sjogren's syndrome: Aberrant expression of APRIL in the salivary gland: J.L. Vosters, et al.; Rheumatology (Oxford) **51,** 1557 (2012) • **[8]** Increased APRIL Expression Induces IgA1 Aberrant Glycosylation in IgA Nephropathy: Y.L. Zhai, et al.; Medicine (Baltimore) **95,** e3099 (2016) • **[9]** The BAFF/APRIL system: an important player in systemic rheumatic diseases: F. Mackay, et al.; Curr. Dir. Autoimmun. **8,** 243 (2005) • **[10]** APRIL, a New Ligand of the Tumor Necrosis Factor Family, Stimulates Tumor Cell Growth: M. Hahne, et al.; J. Exp. Med. **188,** 1185 (1998) • **[11]** In situ detection of APRIL-rich niches for plasma-cell survival and their contribution to B-cell lymphoma development: M. Burjanadze, et al.; Histol. Histopathol. **24,** 1061 (2009) • **[12]** Serum BAFF predicts prognosis better than APRIL in diffuse large B-cell lymphoma patients treated with rituximab plus CHOP chemotherapy: S.J. Kim, et al.; Eur. J. Haematol. **81,** 177 (2008) • **[13]** APRIL limits atherosclerosis by binding to heparan sulfate proteoglycans: D. Tsiantoulas, et al.; Nature **597,** 92 (2021)

AdipoGen® LIFE SCIENCES

Highly Active Proteins – *Manufactured at AdipoGen Life Sciences*

PRODUCT NAME	PID	PRODUCT DESCRIPTION
APRIL (human) (multimeric) (rec.)	AG-40B-0017	MultimericAPRIL™ very effectively stimulates B cell proliferation. This protein binds to human and mouse BCMA and TACI and to proteoglycans.
APRIL (human) (H98) (multimeric) (rec.)	AG-40B-0088	MultimericAPRIL™ very effectively stimulates B cell proliferation. This protein binds to human and mouse BCMA and TACI. Does not bind to proteoglycans.
APRIL (mouse) (multimeric) (rec.)	AG-40B-0089	MultimericAPRIL™ very effectively stimulates B cell proliferation. This protein binds to human and mouse BCMA and TACI and to proteoglycans.
APRIL (mouse) (H98) (multimeric) (rec.)	AG-40B-0035	MultimericAPRIL™ very effectively stimulates B cell proliferation. This protein binds to human and mouse BCMA and TACI. Does not bind to proteoglycans.
UNIQUE **BAFF, Soluble (human) (60-mer) (rec.) (highly active)**	AG-40B-0112	Binds to human and mouse BAFF-R, TACI and BCMA. Increases B cell survival/proliferation. Increases CD21/CD23 expression on B cells *in vivo*. Activates BAFF-R, TACI and BCMA receptors.
BAFF (aa134-285), Soluble (human) (rec.)	AG-40B-0016	Binds to human and mouse BAFF-R, TACI and BCMA.
Fc (human):BAFF (human) (rec.)	AG-40B-0120	Binds to human and mouse BAFF-R, TACI and BCMA. Rescues the production of mature follicular and marginal zone B cells *in vitro* and *in vivo*.
BAFF, Soluble (mouse) (rec.)	AG-40B-0022	Binds to human and mouse BAFF-R, TACI and BCMA.
BAFF-R (human):Fc (human) (rec.)	AG-40B-0027	Binds to human and mouse BAFF. Inhibits BAFF activity.
BCMA (human):Fc (human) (rec.)	AG-40B-0080	Binds mouse and human BAFF and APRIL. Blocks the binding of BAFF and APRIL to their receptors BCMA and TACI, inhibiting BAFF- and APRIL-mediated B cell activation.
BCMA (mouse):Fc (human) (rec.)	AG-40B-0076	Binds mouse and human BAFF and APRIL. Blocks the binding of mouse BAFF and human APRIL to their receptors BCMA and TACI.
TACI (human):Fc (human) (rec.)	AG-40B-0079	Binds to human and mouse BAFF and APRIL. Inhibits BAFF and APRIL activity.

VALIDATED Antibodies for BAFF and APRIL Research

PRODUCT NAME	PID	PRODUCT DESCRIPTION
anti-APRIL (mouse), mAb (rec.) (blocking) (Apry-1-3)	AG-27B-0017	Recognizes mouse APRIL. Does not recognize mouse BAFF. Inhibits the binding of mouse APRIL to BCMA and TACI.
BAFF, Soluble (human) Matched Pair Detection Set	AG-46B-0001	Detects human BAFF in plasma, serum and cell culture supernatant with a sensitivity of 16 pg/ml. Does not detect mouse BAFF.
anti-BAFF (human), mAb (blocking) (4.62)	AG-20B-0017	Recognizes human BAFF. Inhibits human BAFF binding and is used in IP application.
anti-BAFF (human), mAb (2.81)	AG-20B-0018	Recognizes human BAFF and is used in IP application.
anti-BAFF (human), mAb (1-35-1)	AG-20B-0037	Recognizes human BAFF and is used in FACS application.
anti-BAFF (human), mAb (ANC2H3)	ANC-266-020	Recognizes human BAFF. Inhibits human BAFF binding and is used in FACS application.
anti-BAFF-R (human), mAb (HuBR9.1)	AG-20B-0016	Recognizes human BAFF-R. The Standard for FACS application.
anti-BAFF-R (mouse), mAb (9B9)	AG-20B-0034	Recognizes mouse BAFF-R. Used for depletion of B cells *in vivo* and in FACS application.
anti-BAFF-R (human), mAb (ANC268.2/6E6)	ANC-275-020	Recognizes human BAFF-R. Used for FACS application.
anti-BCMA (human), mAb (ANC3B1)	ANC-269-020	Recognizes human BCMA. Used for FACS application.
anti-TACI (mouse), mAb (1A-10)	AG-20B-0035	Recognizes mouse TACI. The Standard for FACS application.

Other Reagents for BAFF and APRIL Research

PRODUCT NAME	PID	PRODUCT DESCRIPTION
anti-LTβR (human), mAb (ANCLTR2/9E2)	ANC-267-020	Recognizes human LTβR. Used in FACS application.
anti-LTβR (mouse), mAb (4H8 WH2) ***BULK available!***	AG-20B-0008	Recognizes mouse LTβR. Agonistic antibody inducing BAFF, chemokines and integrins *in vitro* and *in vivo* and used in FACS application.
anti-LTβR (mouse), mAb (3C8) ***BULK available!***	AG-20B-0041	Recognizes mouse LTβR. Agonistic antibody inducing BAFF, chemokines and integrins *in vitro* and *in vivo* and used in FACS application.
LIGHT, Soluble (human) (rec.)	AG-40B-0009	Binds to human and mouse LTβR and human HVEM and DcR3.
IL-35 (human):Fc (human) (rec.)	CHI-HF-21035	Bioactive in a cell proliferation assay using anti-CD3 activated human peripheral mononuclear cells.
IL-35 (mouse):Fc (human) (rec.)	CHI-MF-11135	Bioactive in a cell proliferation assay of Con A activated mouse splenocytes and in *in vivo* studies.

See www.adipogen.com for all Label Variations and Formats.

Potent BAFF and APRIL Blocking Antibodies

UNIQUE POTENT

anti-BAFF (mouse), mAb (blocking) (Sandy-2)

AG-20B-0063		100 µg
AG-20B-0063PF	Preservative Free	100 µg | 500 µg

This monoclonal antibody recognizes mouse BAFF and works specifically in IP and Functional Application. This antibody inhibits mouse BAFF binding to BAFF-R and TACI. It is highly potent in blocking mouse BAFF *in vivo* and induces B cell depletion and generates a phenotype similar to that observed in BAFF-/- mice.

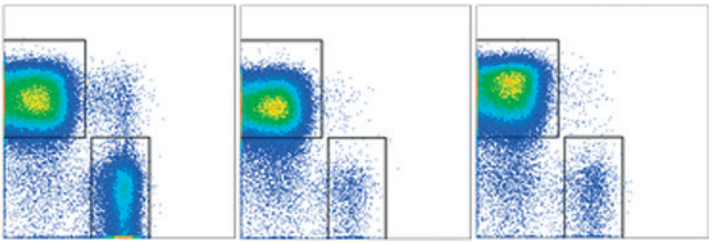


FIGURE: anti-BAFF (mouse), mAb (Sandy-2) (Prod. No. AG-20B-0063) blocks the action of endogenous BAFF *in vivo*.

METHOD: Wild type C57BL/6 mice were treated at day 0 (single administration) with monoclonal antibody anti-BAFF (mouse), mAb (Sandy-2) (at 2mg/kg). Lymph nodes were prepared at week 2 and analyzed by FACS for the presence of T (CD3) and B (CD19) cells. Untreated BAFF WT and KO mice were analyzed in parallel.

anti-APRIL (mouse), mAb (rec.) (blocking) (Apry-1-1)

AG-27B-0001		100 µg
AG-27B-0001PF	Preservative Free	100 µg | 500 µg
AG-27B-0001B	Biotin	100 µg

This recombinant monoclonal antibody recognizes mouse APRIL and works specifically in IP and Functional Application. The antibody inhibits mouse APRIL binding to BCMA and TACI. It is highly potent in blocking mouse APRIL *in vitro* and *in vivo*. In addition it promotes the binding of APRIL to HSPGs and confers atheroprotection.

LIT: APRIL limits atherosclerosis by binding to heparan sulfate proteoglycans: D. Tsiantoulas, et al.; Nature **597,** 92 (2021)

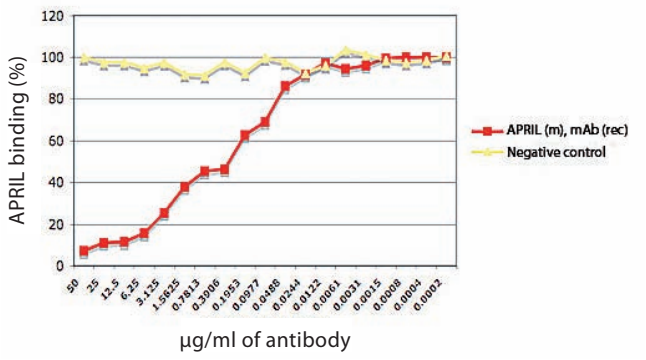


FIGURE: Binding of APRIL (mouse) to BCMA is inhibited by anti-APRIL (mouse), mAb (rec.) (blocking) (Apry-1-1) (Prod. No. AG-27B-0001).

METHOD: BCMA:Fc was coated on an ELISA plate at 1µg/ml. anti-APRIL (mouse) mAb (rec.) (blocking) (Apry-1-1) or an unrelated mAb (recombinant) (Negative control) were added (starting at 50µg/ml with a twofold serial dilution) together with 0.1µg/ml of *Multimeric*APRIL (mouse) (Prod. No. AG-40B-0089). After incubation for 1 h at RT, the *Multimeric*APRIL (mouse) binding was detected using an anti-FLAG® antibody (HRP). The percentage of binding is shown.

NEW

NEW anti-APRIL (mouse), mAb (blocking) (Centotto-1)

AG-20B-0083PF-C100	Preservative Free	100 µg
AG-20B-0083PF-C500	Preservative Free	500 µg

This monoclonal antibody recognizes mouse APRIL and works specifically in IP and Functional Application. This antibody potently depletes mouse APRIL.

LIT: APRIL limits atherosclerosis by binding to heparan sulfate proteoglycans: D. Tsiantoulas, et al.; Nature **597,** 92 (2021)

For a complete overview: https://adipogen.com/autoimmune-diseases-biomarker

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