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β3-chimaerin, a new member of the chimaerin family with a novel SH3 interacting domain

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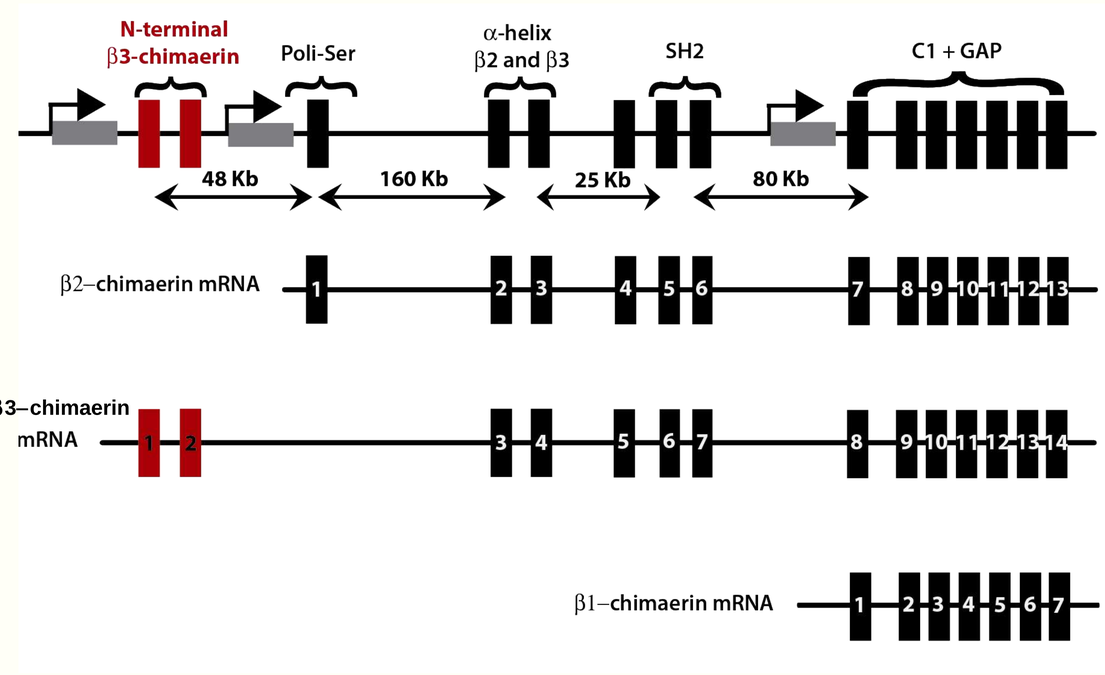
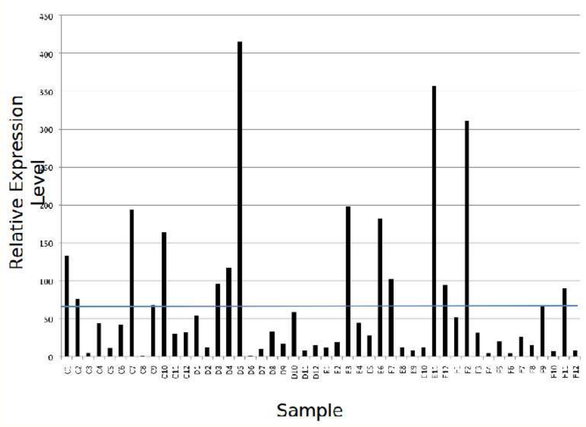
Chimaerins are a family of DAG-modulated regulators of the small GTPase Rac playing a crucial role in development, axon guidance, metabolism, cell migration, and T-cell activation. Four chimaerin isoforms have been reported to-date as products of two chimaerin genes: CHN1 (alpha1 and 2) and CHN2 (beta1 and 2). The known products of these genes are assumed to be generated by alternative splicing.



Bioinformatic analysis of the CHN2 gene revealed that these β1 and β2 are the product of alternate transcription start sites regulated by different promoter regions.

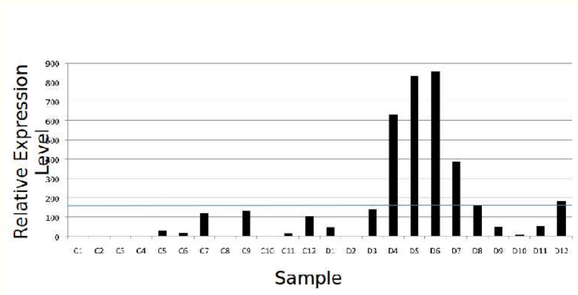
We report the cloning and functional characterization of β3-chimaerin, the product of an additional transcription star site 80 Kb upstream CHN2.

The expression profile of β3-chimaerin was analyzed by Real Time PCR using a hole body cDNA array, showing higher levels of mRNA in epididymis, plasma blood leucocytes, spleen and thymus.



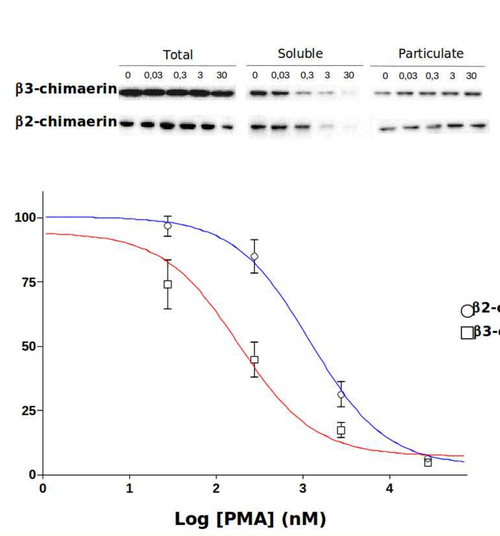
Location	Tissue	Location	Tissue
C-1	Adrena Gland	E-1	Penis
C-2	Bone Marrow	E-2	Pericardium
C-3	Brain	E-3	Pituitary
C-4	Cervix	E-4	Placenta
C-5	Colon	E-5	Prostate
C-6	Descending part of duodenum	E-6	Rectum
C-7	Epididymis	E-7	Retina
C-8	Esophagus	E-8	Seminal Vesicles
C-9	Fat	E-9	Skin
C-10	Heart	E-10	Spinal Cord
C-11	Intestine (Small)	E-11	Spleen
C-12	Intracranial Artery	E-12	Stomach
D-1	Kidney	F-1	Testis
D-2	Liver	F-2	Thymus
D-3	Lung	F-3	Thyroid
D-4	Lymph Node	F-4	Tongue
D-5	PBL (plasma blood leucocytes)	F-5	Tonsil
D-6	Mammary gland	F-6	Trachea
D-7	Muscle	F-7	Urethra
D-8	Nasal Mucosa	F-8	Urinary Bladder
D-9	Optic Nerve	F-9	Uterus
D-10	Ovary	F-10	Uvula
D-11	Oviduct	F-11	Vagina
D-12	Pancreas	F-12	Vena Cava

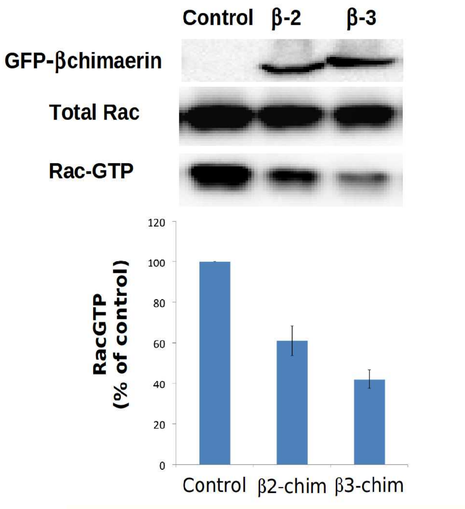
Using a brain cDNA array we also detected high levels of expression in the pituitary gland, cerebellum grey, cerebellum white and vermis.



Location	Tissue	Location	Tissue
C-1	Frontal Lobe	D-1	Caudate
C-2	Temporal Lobe	D-2	Putamen
C-3	Occipital Lobe	D-3	Substantia Nigra
C-4	Parietal Lobe	D-4	Pituitary Gland
C-5	Paracentral Gyrus	D-5	Cerebellum grey
C-6	Postcentral Gyrus	D-6	Cerebellum white
C-7	Olfactory Bulb	D-7	Cerebellum vermis
C-8	Thalamus	D-8	Nucleus Accumbens
C-9	Corpus Callosum	D-9	Pons
C-10	Hypothalamus	D-10	Medulla
C-11	Amygdala	D-11	Spinal Cord
C-12	Hippocampus	D-12	Choroid Plexus

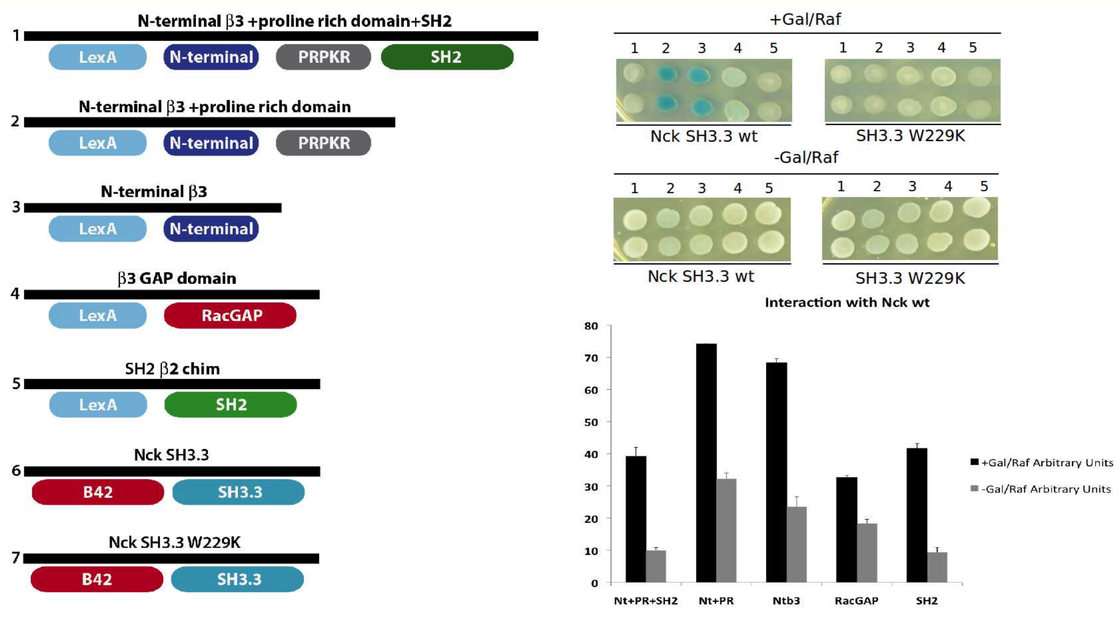
β3-chimaerin differs from β2-cimaerin on its N-terminal domain, being 7 times more sensitive to PMA-induced translocation and possessing higher Rac-GAP activity.





β3-chimaerin's N-terminal domain is only conserved in chimpanzees and has no sequence identity to any other known protein.

Using a yeast two hybrid assay we proved that this novel domain interacts with Nck third SH3 domain.



β3-chimaerin N-terminus represents a novel SH3-interacting domain.