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26 April 2000

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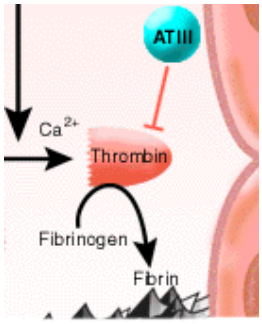

A cascade of clotting factors culminates in the formation of a blood clot.

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Mutations and blood clots

Clotting is essential, yet can be fatal. Pathological activation of the clotting cascade can lead to the formation of a blood clot, typically a deep vein thrombosis (DVT) in the legs. This blood clot may then be carried in the bloodstream to the lungs. This is known as a pulmonary embolism and is a medical emergency, being one of the leading causes of sudden death.

After trauma, the formation of a thrombus is essential to stem bleeding. A cascade of pro-enzymes, enzymes and cofactors interact with damaged vessel endothelium to converge on a common pathway with the formation of a fibrin clot. The clot acts a mechanical plug to prevent bleeding and is vital for normal vascular function. Disturbance of this pathway can be deadly - too little clotting results in bleeding disorders such as hemophilia, whereas excessive clotting produces blood clots that can block the lungs.

There are many factors that lead to an excessive propensity to clot, or thrombophilia. These can be classified by: (1) changes in blood vessel wall (2) changes in blood flow and (3) changes in blood constituents. Among the genetic components that underlie problems with blood constituents are mutations of clotting factor genes. These cause a deficiency of the body's natural anticoagulants, such as protein C, protein S, or antithrombin III (see figure). However, the most common inherited mutation that predisposes to thrombosis is the factor V Leiden mutation.

Factor V acts towards the end of the clotting cascade, where it is a co-factor for the Xa-dependant proteolytic cleavage of prothrombin to thrombin. Thrombin then catalyzes the conversion of soluble fibrinogen to a solid fibrin clot. Activated factor V (Va) is kept in check by a serine protease called activated protein C (APC). APC stops factor V from working by cleaving sites on its heavy chain - in particular at the sites Arg506 and Arg306. Thus APC is important in limiting clot formation.

Factor V Leiden is a single point mutation resulting in an amino acid substitution of arginine for glutamine at Arg506. The mutation affects factor V's APC-binding site, therefore preventing factor V inactivation. It is carriers of this APC-resistant factor V that suffer from a propensity to inappropriate clot formation.

What if you are a carrier of factor V Leiden? It is a common mutation, with a prevalence of 2% in Caucasian populations. It is especially found in patients with DVTs and increases the risk of thrombosis during pregnancy or while taking oral contraceptives. It is also associated with an increased risk of miscarriage. Although it is the most important genetic risk factor that we know of, the overall probability of thrombosis is still low with a single mutation. However, with the co-inheritance of other clotting factor polymorphisms

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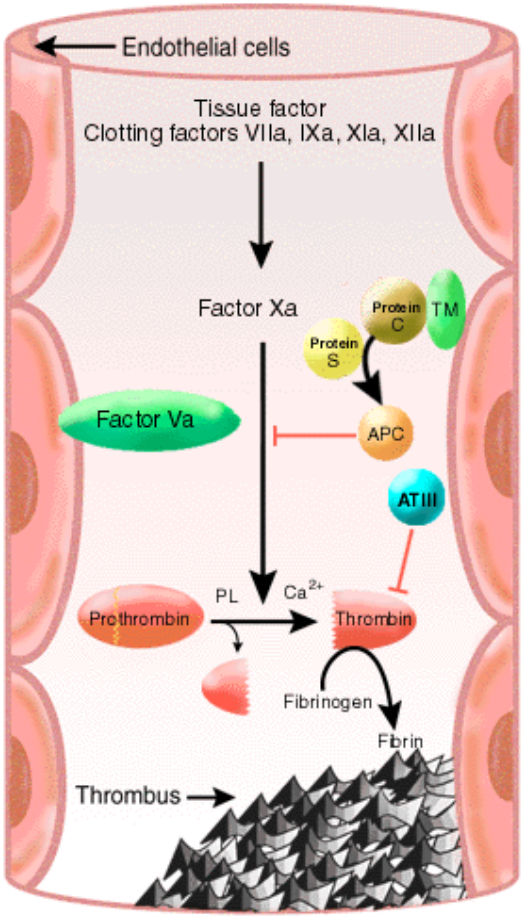
such as that of prothrombin which increases levels of prothrombin in the blood, the risk of thrombosis now becomes more significant.

Further investigation of the clotting factor mutations will help explain the hereditary basis of thrombophilia. Most importantly however, the main causes of DVT are not inherited but are acquired. Despite our genetic make-up, a healthy lifestyle is our most important weapon for keeping thrombosis at bay.

Figure **Coffee Break**

Mutations and blood clots



Key
Black arrows = activation;
Red arrows = inactivation;
APC = activated protein C
TM = thrombomodulin, a protein bound to endothelial cell membranes to which protein C binds;
PL = phospholipid;
Ca^{2+} = calcium;

Each reaction in the coagulation cascade involves the conversion of a clotting factor precursor into an active protease by proteolysis, regulated by cofactors and calcium. The end point is the generation of enough thrombin to catalyze the formation of fibrin, which then polymerizes and crosslinks to form a clot. Under pathological conditions, the mutation in **factor V** renders it resistant to inactivation by APC. Hence mutated factor V pushes the cascade towards excessive blood clot formation. Mutations in the upstream region of the **prothrombin** gene result in increased levels of prothrombin in the blood, again encouraging the formation of a thrombus. Protein C, protein S and antithrombin III all have anti-coagulant action. Deficiencies of proteins C and S usually result in a syndrome of recurrent venous thrombosis and pulmonary embolism. Deficiency of antithrombin III is usually mild.

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Venous thromboembolism are major causes of disease and death in pregnancy. To search PubMed for articles on this topic, the following search terms have been entered in the textbox above. Now click on 'Go'.

PubMed is the National Library of Medicine's search service that provides access to over 10 million citations in MEDLINE, PreMEDLINE, and other related databases, with links to participating online journals.

The second article in the list below is about the effect of excessive clotting on both the pregnant mother and the fetus. Use the 'Related Articles' function to find more articles on this topic.

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1 : Durnwald CP, Flora R, Agamanolis D, Spirtos N, Steele M, Galehouse D. Related Articles
Hereditary thrombophilia as a cause of fetal loss.
Obstet Gynecol. 2000 Apr 1;95(4 Suppl 1):S11-S12.
[Record as supplied by publisher]
PMID: 10729421

2 : Greer IA. Related Articles
The challenge of thrombophilia in maternal-fetal medicine.
N Engl J Med. 2000 Feb 10;342(6):424-5. No abstract available.
PMID: 10666435; UI: 20116960

3 : Gerhardt A, Scharf RE, Beckmann MW, Struve S, Bender HG, Pillny M, Sandmann W, Zotz RB. Related Articles
Prothrombin and factor V mutations in women with a history of thrombosis during pregnancy and the puerperium.
N Engl J Med. 2000 Feb 10;342(6):374-80.
PMID: 10666427; UI: 20116952

4 : Foka ZJ, Lambropoulos AF, Saravelos H, Karas GB, Karavida A, Agorastos T, Zournatzi V, Makris PE, Bontis J, Kotsis A. Related Articles
Factor V leiden and prothrombin G20210A mutations, but not methylenetetrahydrofolate reductase C677T, are associated with recurrent miscarriages.
Hum Reprod. 2000 Feb;15(2):458-62.
PMID: 10655323; UI: 20122400

5 : Lockwood CJ. Related Articles
Heritable coagulopathies in pregnancy.
Obstet Gynecol Surv. 1999 Dec;54(12):754-65. Review.
PMID: 10596396; UI: 20064193

6 : Blumenfeld Z, Brenner B. Related Articles
Thrombophilia-associated pregnancy wastage.
Fertil Steril. 1999 Nov;72(5):765-74. Review.
PMID: 10560975; UI: 20023631

7 : Frenkel EP, Bick RL. Related Articles
Prothrombin G20210A gene mutation, heparin cofactor II defects, primary (essential) thrombocythemia, and thrombohemorrhagic manifestations.
Semin Thromb Hemost. 1999;25(4):375-86. Review.
PMID: 10548071; UI: 20014107

8 : Eichinger S, Weltermann A, Philipp K, Hafner E, Kaider A, Kittl EM, Brenner B, Mannhalter C, Lechner K, Kyrle PA. Related Articles
Prospective evaluation of hemostatic system activation and thrombin potential in healthy pregnant women with and without factor V Leiden.
Thromb Haemost. 1999 Oct;82(4):1232-6.
PMID: 10544904; UI: 20010988

9 : Martinelli I, Cattaneo M, Taioli E, De Stefano V, Chiusolo P, Mannucci PM. Related Articles
Genetic risk factors for superficial vein thrombosis.
Thromb Haemost. 1999 Oct;82(4):1215-7.
PMID: 10544900; UI: 20010984

10 : Souza SS, Ferriani RA, Pontes AG, Zago MA, Franco RF. Related Articles
Factor V leiden and factor II G20210A mutations in patients with recurrent abortion.
Hum Reprod. 1999 Oct;14(10):2448-50.
PMID: 10527966; UI: 99459329

11 : De Groot CJ, Bloemenkamp KW, Duvekot EJ, Helmerhorst FM, Bertina RM, Van Der Meer F, De Ronde H, Oei SG, Kanhai HH, Rosendaal FR. Related Articles
Preeclampsia and genetic risk factors for thrombosis: a case-control study.
Am J Obstet Gynecol. 1999 Oct;181(4):975-80.
PMID: 10521764; UI: 99452652

12 : Verdy E, Berkane N, Magdelaine A, Soubrier F, Uzan S. Related Articles

[Prevalence of factor V Leiden, hyperhomocysteinemia, prothrombin G20210A, and methylene tetrahydrofolate reductase C677T mutations in obstetrical complications].

Ann Biol Clin (Paris). 1999 Sep-Oct;57(5):539-44. Review. French.
PMID: 10518055; UI: 99447410

13 : van Boven HH, Vandenbroucke JP, Briet E, Rosendaal FR. Related Articles

Gene-gene and gene-environment interactions determine risk of thrombosis in families with inherited antithrombin deficiency.

Blood. 1999 Oct 15;94(8):2590-4.
PMID: 10515862; UI: 99445368

14 : Brenner B, Sarig G, Weiner Z, Younis J, Blumenfeld Z, Lanir N. Related Articles

Thrombophilic polymorphisms are common in women with fetal loss without apparent cause.

Thromb Haemost. 1999 Jul;82(1):6-9.
PMID: 10456445; UI: 99383348

15 : McColl MD, Walker ID, Greer IA. Related Articles

The role of inherited thrombophilia in venous thromboembolism associated with pregnancy.

Br J Obstet Gynaecol. 1999 Aug;106(8):756-66. Review.
PMID: 10453824; UI: 99381627

16 : Verspyck E, Le Cam-Duchez V, Gravier A, Descargues G, Marpeau L, Borg JY. Related Articles

Small for gestational age infant in association with maternal prothrombin gene variant (nt 20210A).

Eur J Obstet Gynecol Reprod Biol. 1999 Apr;83(2):143-4.
PMID: 10391523; UI: 99318407

17 : Wisotzkey JD, Bayliss P, Rutherford E, Bell T. Related Articles

Placental genotyping of the factor V Leiden, prothrombin 20210A and the methylenetetrahydrofolate reductase (MTHFR) C677T alleles in IUGR pregnancies.

Thromb Haemost. 1999 May;81(5):844-5. No abstract available.
PMID: 10365762; UI: 99291884

18 : Marcucci R, Abbate R, Fedi S, Gori AM, Brunelli T, Bruni V, Bucciantini S, Micheli S, Pepe G, Prisco D, Gensini GF. Related Articles

Acquired activated protein C resistance in postmenopausal women is dependent on factor VIII:c levels.

Am J Clin Pathol. 1999 Jun;111(6):769-72.
PMID: 10361512; UI: 99289862

19 : Kutteh WH, Park VM, Deitcher SR. Related Articles

Hypercoagulable state mutation analysis in white patients with early first-trimester recurrent pregnancy loss.

Fertil Steril. 1999 Jun;71(6):1048-53.
PMID: 10360908; UI: 99287653

20 : Chrobak L, Dulicek P. Related Articles

[Thrombophilic states].

Vnitr Lek. 1998 Aug;44(8):481-6. Review. Czech.
PMID: 10358455; UI: 99286497

Revised: December 3, 1999.

The fifth article listed here is concerned with factor V and prothrombin mutations causing thrombosis during pregnancy and for a period of time after delivery. Click on this article to view the abstract.

1 : Durnwald CP, Flora R, Agamanolis D, Spirtos N, Steele M, Galehouse D. Related Articles
Hereditary thrombophilia as a cause of fetal loss.
Obstet Gynecol. 2000 Apr 1;95(4 Suppl 1):S11-S12.
[Record as supplied by publisher]
PMID: 10729421

2 : Younis JS, Brenner B, Ohel G, Tal J, Lanir N, Ben-Ami M. Related Articles
Activated protein C resistance and factor V Leiden mutation can be associated with first-as well as second-trimester recurrent pregnancy loss.
Am J Reprod Immunol. 2000 Jan;43(1):31-5.
[MEDLINE record in process]
PMID: 10698038; UI: 20161864

3 : Tormene D, Simioni P, Prandoni P, Luni S, Innella B, Sabbion P, Girolami A. Related Articles
The risk of fetal loss in family members of probands with factor V Leiden mutation.
Thromb Haemost. 1999 Oct;82(4):1237-9.
PMID: 10544905; UI: 20010989

4 : Ridker PM, Miletich JP, Buring JE, Ariyo AA, Price DT, Manson JE, Hill JA. Related Articles
Factor V Leiden mutation as a risk factor for recurrent pregnancy loss.
Ann Intern Med. 1998 Jun 15;128(12 Pt 1):1000-3.
PMID: 9625662; UI: 98273837

5 : Gerhardt A, Scharf RE, Beckmann MW, Struve S, Bender HG, Pillny M, Sandmann W, Zotz RB. Related Articles
Prothrombin and factor V mutations in women with a history of thrombosis during pregnancy and the puerperium.
N Engl J Med. 2000 Feb 10;342(6):374-80.
PMID: 10666427; UI: 20116952

6 : Brenner B, Sarig G, Weiner Z, Younis J, Blumenfeld Z, Lanir N. Related Articles
Thrombophilic polymorphisms are common in women with fetal loss without apparent cause.
Thromb Haemost. 1999 Jul;82(1):6-9.
PMID: 10456445; UI: 99383348

7 : Kutteh WH, Park VM, Deitcher SR. Related Articles
Hypercoagulable state mutation analysis in white patients with early first-trimester recurrent pregnancy loss.
Fertil Steril. 1999 Jun;71(6):1048-53.
PMID: 10360908; UI: 99287653

8 : Dulicek P, Chrobak L, Kalousek I, Pesavova L, Pecka M, Stransky P. Related Articles
Is factor V Leiden a risk factor for fetal loss?
Acta Medica (Hradec Kralove). 1999;42(3):93-6.
PMID: 10677895; UI: 20142385

9 : Foka ZJ, Lambropoulos AF, Saravelos H, Karas GB, Karavida A, Agorastos T, Zournatzi V, Makris PE, Bontis J, Kotsis A. Related Articles
Factor V leiden and prothrombin G20210A mutations, but not methylenetetrahydrofolate reductase C677T, are associated with recurrent miscarriages.
Hum Reprod. 2000 Feb;15(2):458-62.
PMID: 10655323; UI: 20122400

10 : Mello G, Parretti E, Martini E, Mecacci F, La Torre P, Cioni R, Lucchetti R, Fedi S, Gori AM, Pepe G, Prisco D, Abbate R. Related Articles
Usefulness of Screening for Congenital or Acquired Hemostatic Abnormalities in Women with Previous Complicated Pregnancies.
Haemostasis. 1999 Dec;29(4):197-203.
[Record as supplied by publisher]
PMID: 10702700

11 : Tal J, Schliamser LM, Leibovitz Z, Ohel G, Attias D. Related Articles
A possible role for activated protein C resistance in patients with first and second trimester pregnancy failure.

Hum Reprod. 1999 Jun;14(6):1624-7.
PMID: 10357988; UI: 99287993

12 : De Stefano V, Martinelli I, Mannucci PM, Paciaroni K, Chiusolo P, Casorelli I, Rossi E, Leone G. Related Articles
The risk of recurrent deep venous thrombosis among heterozygous carriers of both factor V Leiden and the G20210A prothrombin mutation.
N Engl J Med. 1999 Sep 9;341(11):801-6.
PMID: 10477778; UI: 99393045

13 : Grandone E, Margaglione M, Colaizzo D, D'Andrea G, Cappucci G, Brancaccio V, Di Minno G. Related Articles
Genetic susceptibility to pregnancy-related venous thromboembolism: roles of factor V Leiden, prothrombin G20210A, and methylenetetrahydrofolate reductase C677T mutations.
Am J Obstet Gynecol. 1998 Nov;179(5):1324-8.
PMID: 9822524; UI: 99039977

14 : Meinardi JR, Middeldorp S, de Kam PJ, Koopman MM, van Pampus EC, Hamulyak K, Prins MH, Buller HR, van der Meer J. Related Articles
Increased risk for fetal loss in carriers of the factor V Leiden mutation.
Ann Intern Med. 1999 May 4;130(9):736-9.
PMID: 10357692; UI: 99223111

15 : Murphy RP, Donoghue C, Nallen RJ, D'Mello M, Regan C, Whitehead AS, Fitzgerald DJ. Related Articles
Prospective evaluation of the risk conferred by factor V Leiden and thermolabile methylenetetrahydrofolate reductase polymorphisms in pregnancy.
Arterioscler Thromb Vasc Biol. 2000 Jan;20(1):266-70.
PMID: 10634828; UI: 20102891

16 : Huisman MV, Rosendaal F. Related Articles
Thrombophilia.
Curr Opin Hematol. 1999 Sep;6(5):291-7. Review.
PMID: 10468143; UI: 99396219

17 : van Leeuwen I, Branch DW, Scott JR. Related Articles
First-trimester ultrasonography findings in women with a history of recurrent pregnancy loss.
Am J Obstet Gynecol. 1993 Jan;168(1 Pt 1):111-4. Review.
PMID: 8420310; UI: 93128367

18 : Grandone E, Margaglione M, Colaizzo D, d'Addedda M, Cappucci G, Vecchione G, Scianname N, Pavone G, Di Minno G. Related Articles
Factor V Leiden is associated with repeated and recurrent unexplained fetal losses.
Thromb Haemost. 1997 May;77(5):822-4.
PMID: 9184385; UI: 97327793

19 : Rintelen C, Mannhalter C, Lechner K, Eichinger S, Kyrle PA, Papagiannopoulos M, Schneider B, Pabinger I. Related Articles
No evidence for an increased risk of venous thrombosis in patients with factor V Leiden by the homozygous 677 C to T mutation in the methylenetetrahydrofolate-reductase gene.
Blood Coagul Fibrinolysis. 1999 Mar;10(2):101-5.
PMID: 10192659; UI: 99206877

20 : Holmes ZR, Regan L, Chilcott I, Cohen H. Related Articles
The C677T MTHFR gene mutation is not predictive of risk for recurrent fetal loss.
Br J Haematol. 1999 Apr;105(1):98-101.
PMID: 10233370; UI: 99250510

Revised: December 3, 1999.

This is a paper which studies the incidence of thrombosis in women during pregnancy and for a 6 week period after giving birth. It found that of the women who suffered from a deep vein thrombosis during this period, a significant proportion had underlying genetic abnormalities. It indicates the risk of thromboembolism for prothombin mutations is at least as high for that of factor V leiden. A risk of thrombosis as high as 69% was estimated if both these mutations were co-inherited.

1 : *N Engl J Med* 2000 Feb 10;342(6):374-80

Related Articles, Books, LinkOut

NEJM

Prothrombin and factor V mutations in women with a history of thrombosis during pregnancy and the puerperium.

Gerhardt A, Scharf RE, Beckmann MW, Struve S, Bender HG, Pillny M, Sandmann W, Zotz RB

Department of Hemostasis and Transfusion Medicine, Heinrich Heine University Medical Center, Dusseldorf, Germany.

BACKGROUND: Venous thromboembolism is a leading cause of morbidity and mortality during pregnancy and the puerperium. However, the role of mutations in the prothrombin and factor V genes and other thrombophilic abnormalities as risk factors for thromboembolism in women during pregnancy and the pueperium is not known. METHODS: In a study of 119 women with a history of venous thromboembolism during pregnancy and the puerperium and 233 age-matched normal women, we measured the activity of antithrombin, protein C, protein S, and lupus anticoagulant. We also performed genetic analyses to detect the G1691A mutation in the factor V gene (factor V Leiden), the G20210A mutation in the prothrombin gene, and the C677T mutation in the methylenetetrahydrofolate reductase gene. Blood samples were obtained at least three months post partum or after the cessation of lactation. RESULTS: Among the women with a history of venous thromboembolism, the prevalence of factor V Leiden was 43.7 percent, as compared with 7.7 percent among the normal women (relative risk of venous thromboembolism, 9.3; 95 percent confidence interval, 5.1 to 16.9); that of the G20210A prothrombin-gene mutation, 16.9 percent as compared with 1.3 percent (relative risk, 15.2; 95 percent confidence interval, 4.2 to 52.6); and that of both factor V Leiden and the G20210A prothrombin-gene mutation 9.3 percent as compared with 0 (estimated odds ratio, 107). Assuming an overall risk of 1 in 1500 pregnancies, the risk of thrombosis among carriers of factor V Leiden was 0.2 percent, among carriers of the G20210A prothrombin-gene mutation, 0.5 percent, and among carriers of both defects, 4.6 percent, as calculated in a multivariate analysis. CONCLUSIONS: The G20210A prothrombin-gene mutation and factor V Leiden individually are associated with an increased risk of venous thromboembolism during pregnancy and the puerperium, and the risk among women with both mutations is disproportionately higher than that among women with only one mutation.

Comments:
- Comment in: N Engl J Med 2000 Feb 10;342(6):424-5

PMID: 10666427, UI: 20116952

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Revised: January 10, 2000.

NCBI *MMDB* STRUCTURE SUMMARY Entrez ?

To view the 3D structure of the C2 membrane binding domain of factor V:
Download the latest version of the viewer
The Cn3D viewer enables you to interactively view the 3D structure of macromolecules. You can zoom in on the structure, rotate, annotate and highlight the residues you are interested in.

MMDB Id: 11477 PDB Id: 1CZT

Protein Chains: A
MEDLINE: PubMed
Taxonomy: A Homo sapiens

PDB Authors: S.Macedo-Ribeiro, W.Bode, R.Huber, W.H.Kane & P.Fuentes-Prior
PDB Deposition: 7-Sep-99
PDB Class: Blood Clotting
PDB Title: Crystal Structure Of The C2 Domain Of Human Coagulation Factor V

Sequence Neighbors: A
Structure Neighbors: A

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Options:	**Viewer:**	**Complexity:**	
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( ) See File	( ) Cn3D v1.0 (asn.1)	( ) Virtual Bond Model	( ) Up to 10 Models
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Mus musculus

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Danio rerio

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dbEST-Database of Expressed Sequence Tags

Cancer Genome Anatomy Project

UniGene is a collection of Genbank sequences that have been organized into clusters - the aim is for each cluster to represent one gene. Expressed Sequence Tags (ESTs) make up most of the clusters. These are short nucleotide sequences (100-400 nt) and so represent only fragments of genes. ESTs are selected and sequenced at random from cDNA libraries derived from a cell line or tissue of interest e.g. a cell line from a family with hereditary thrombophilia. Such rapid production of ESTs enables a much faster rate of progress of gene discovery.

Coagulation factor V has been entered in the text box, click on "go".

UniGene Resources

The UniGene System

UniGene is an experimental system for automatically partitioning GenBank sequences into a non-redundant set of gene-oriented clusters. Each UniGene cluster contains sequences that represent a unique gene, as well as related information such as the tissue types in which the gene has been expressed and map location.

In addition to sequences of well-characterized genes, hundreds of thousands novel expressed sequence tag (EST) sequences have been included. Consequently, the collection may be of use to the community as a resource for gene discovery. UniGene has also been used by experimentalists to select reagents for gene mapping projects and large-scale expression analysis.

However, it should be noted that the procedures for automated sequence clustering are still under development and the results may change from time to time as improvements are made. Feedback from users has been especially useful in identifying problems and we encourage you to report any problems you encounter.

It should also be noted that no attempt has been made to produce contigs or consensus sequences. There are several reasons why the sequences of a set may not actually form a single contig. For example, all of the splicing variants for a gene are put into the same set. Moreover, EST-containing sets often contain 5' and 3' reads from the same cDNA clone, but these sequences do not always overlap.

At present, only sequences from human, rat, and mouse have been processed. These species were chosen because they have the greatest amounts of EST data available. Additional organisms may be added in the future.

A representation of the UniGene datasets is available by **ftp** .

A description of the UniGene **build procedure** is available.

UniGene References

An article about the **UniGene Collection** in the **August 1997 NCBI News** contains an overview of the project. Although the number of UniGene clusters has changed since that article was written due to improvements in the clustering algorithm, the article provides background information as well as a description of how the collection was used in the Transcript Map project (see Schuler et al., 1996, below).

Additional references include:

Schuler (1997). Pieces of the puzzle: expressed sequence tags and the catalog of human genes. J Mol Med 75(10),694-698. [**PubMed**]

Schuler et al. (1996). A gene map of the human genome. Science 274, 540-546. [**PubMed**] [**SCIENCE On-line**]

Boguski & Schuler (1995). ESTablishing a human transcript map. Nature Genetics 10, 369-371. [**PubMed**] [**Full Text**]

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Homo sapiens

Release Statistics

Weekly Library Report

Library Differential Display

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dbEST-Database of Expressed Sequence Tags

Cancer Genome Anatomy Project

Click on the UniGene reference number for coagulation factor V.

2 records satisfy the query **coagulation factor v** for the organism **Homo sapiens**

UniGene	Description	Symbol
Hs.21016	coagulation factor C (Limulus polyphemus) homology (cochlin)	COCH
Hs.30054	coagulation factor V (proaccelerin, labile factor)	F5

Hs.30054 *Homo sapiens* **F5**

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dbEST-Database of Expressed Sequence Tags

Cancer Genome Anatomy Project

Gene hunters use UniGene for discovering new family members of their gene of interest in the same species, and for finding functionally equivalent genes in other species. We are interested in the factor V protein. There is a similar protein in the fruit fly called neurexin IV. This protein has a stretch of 124 amino acids that have a 31% identity to human factor V protein. Click on the protein identifier (PID) to find out about the function of neurexin.

Coagulation factor V (proaccelerin, labile factor)

SEE ALSO

LocusLink: 2153
OMIM: 227400

SELECTED MODEL ORGANISM PROTEIN SIMILARITIES

H. sapiens :	PID:g488110 - coagulation factor V	**100 % / 2223 aa**
M. musculus :	PID:g3219691 - Murine coagulation factor V	**70 % / 2219 aa**
R. norvegicus :	PIR:A35210 - ferroxidase	**36 % / 623 aa**
D. melanogaster :	PID:g1518221 - neurexin IV	**31 % / 124 aa**
C. elegans :	PID:g1086659 - repetitive region	**30 % / 247 aa**
S. cerevisiae :	PID:e239834 - ORF YNR044w	**25 % / 276 aa**

MAPPING INFORMATION

Chromosome: 1
Cytogenetic Position: 1q23
Gene Map 98: Marker stGDB:194742 , Interval D1S196-D1S210
Gene Map 98: Marker M14335 , Interval D1S196-D1S210
Gene Map 98: Marker W88564 , Interval D1S196-D1S210
Gene Map 98: Marker SGC32933 , Interval D1S196-D1S210
Gene Map 98: Marker stSG17607 , Interval D1S196-D1S210
Whitehead map: EST376226, Chr.1
dbSTS entries: G25791

EXPRESSION INFORMATION

cDNA sources: Liver and Spleen, gall bladder, heart, kidney, lung, placenta, prostate
SAGE : Gene to Tag mapping

mRNA/GENE SEQUENCES (5)

L32779	Human coagulation factor V gene	P A S
M16967	Human coagulation factor V mRNA, complete cds	P A S
M14335	Human coagulation factor V mRNA, complete cds	P A S
Z99572	Human DNA sequence from PAC 86F14 on chromosome 1q23-1q24. Contains coagulation factor V, ESTs and STS	P S
NM_000130	Homo sapiens coagulation factor V (proaccelerin, labile factor) (F5) mRNA	

EST SEQUENCES (10 of 50)[Show all ESTs]

AI207246	cDNA clone IMAGE:1758878		3' read	1.3 kb	P C
AI274530	cDNA clone IMAGE:1981178	Kidney	3' read	1.2 kb	P A C
R84234	cDNA clone IMAGE:194571		5' read	1.2 kb	P
R71060	cDNA clone IMAGE:142726	Placenta	3' read	1.2 kb	S
H74282	cDNA clone IMAGE:229509		5' read	1.1 kb	P S
H74283	cDNA clone IMAGE:229509		3' read	1.1 kb	P S
AA976662	cDNA clone IMAGE:1585363	Lung	3' read	1.1 kb	P A S C
H75674	cDNA clone IMAGE:211332		5' read	1.0 kb	P
H69028	cDNA clone IMAGE:211332		3' read	1.0 kb	P A S
H78713	cDNA clone IMAGE:229431		5' read	1.0 kb	P

Key to Symbols

P Has similarity to known **P**roteins (after translation)
A Contains a poly-**A**denylation signal
S Contains a mapped **S**equence-tagged site (STS)
C Clone source is a **C**GAP library

Download sequences

Questions or comments?
Write to the NCBI Service Desk

Whereas factor V is a clotting factor, neurexin is a protein involved in the blood brain barrier in the fly. To find out more about neurexin and to find whether there is any correlation of function with that of factor V, click on the medline reference number.

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1 : CAA60383 . (X86685) neurexin ...[gi:1518221]

PubMed, Related Sequences, Nucleotide, LinkOut

```
LOCUS       CAA60383     1283 aa                    INV       14-JAN-1997
DEFINITION  neurexin IV [Drosophila melanogaster].
ACCESSION   CAA60383
PID         g1518221
VERSION     CAA60383.1  GI:1518221
DBSOURCE    embl locus DMNRXGENE, accession X86685.1
KEYWORDS    .
SOURCE      fruit fly.
  ORGANISM  Drosophila melanogaster
            Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;
            Pterygota; Diptera; Brachycera; Muscomorpha; Ephydroidea;
            Drosophilidae; Drosophila.
REFERENCE   1  (residues 1 to 1283)
  AUTHORS   Baumgartner,S., Littleton,J.T., Broadie,K., Bhat,M.A., Harbecke,R.,
            Lengyel,J.A., Chiquet-Ehrismann,R., Prokop,A. and Bellen,H.J.
  TITLE     A Drosophila neurexin is required for septate junction and
            blood-nerve barrier formation and function
  JOURNAL   Cell 87 (6), 1059-1068 (1996)
MEDLINE     97133213
REFERENCE   2  (residues 1 to 1283)
  AUTHORS   Baumgartner,S.W.
  TITLE     Direct Submission
  JOURNAL   Submitted (26-APR-1995) S.W. Baumgartner, FMI, PO Box 2543, 4002
            Basel, SWITZERLAND
FEATURES             Location/Qualifiers
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     sig_peptide     1..28
     CDS             1..1283


                     /gene="nrx"
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                     /db_xref="SPTREMBL:Q94887"
                     /coded_by="X86685.1:279..4130"


ORIGIN
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      121 ysddgefwrs yvnptsepqm fkgnsdgnsi hynvfevpii aqwvrinptr whdrismrve
      181 lygcdyisen lyfngtglvr ydlrrepits tkesirfrfk tafangvmmy srgtqgdyya
      241 lqlkdnkmvl nldlgsrvmt slsvgslldd nvwhdvvisr nqrdiifsvd rvivrgriqg
      301 eftrlnlnre lylggvpnvq eglivqqnfs gcleniyfns tnfirvmkds telgegylft
      361 rvntiyacps ppiypvtftt rssfvrlkgy ensqrlnvsf yfrtyeetgv mlhhdfysgg
      421 ylkvflefgk vkidlkvkdk ariildnydd qfndgkwhsf visieknrli lnidqrpmtt
      481 tksmqvatga qyyiaggkdk ngfvgcmrli svdgnyklpq dwvkgeevcc gddvvvdacq
      541 midrcnpnpc qhkglchqns reffcdcght gyagavchts nnplsclalk nvqhvqqrvn
      601 lnldvdgsgp lepfpvtcef ysdgrvittl shsqehtttv dgfqepgsfe qsimydanql
      661 qieallnrsh scwqrlsysc rssrlfnsps eagnfrpfsw wisrhnqpmd ywagalpgsr
      721 kcecgilgkc hdptkwcncd snslewmedg gdirekeylp vravkfgdtg tpldekmgry
      781 tlgplrcegd dlfsnvvtfr iadasinlpp fdmghsgdiy lefrttqens vifhatgptd
      841 yiklslnggn klqfqyqags gplgvnvgts yhlndnnwht vsvernrkea rlvvdgsika
      901 evreppgpvr alhltsdlvi gattdyrdgy vgcirallln gkmvdlkeys krglygistg
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     1261 dpddavlhst tghqvrkrte ifi
//
```

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Revised: January 10, 2000.

Neurexin IV is a protein needed for the proper formation of junctions and barriers between cells. Perhaps the amino acid sequence similarity that is observed in the fly neurexin protein and human factor V represents a common domain that is important in cell binding.

1 : *Cell* 1996 Dec 13;87(6):1059-68 Related Articles, Books, Protein, Nucleotide, LinkOut

A Drosophila neurexin is required for septate junction and blood-nerve barrier formation and function.

Baumgartner S, Littleton JT, Broadie K, Bhat MA, Harbecke R, Lengyel JA, Chiquet-Ehrismann R, Prokop A, Bellen HJ

Friedrich Miescher-Institute, Basel, Switzerland.

Septate and tight junctions are thought to seal neighboring cells together and to function as barriers between epithelial cells. We have characterized a novel member of the neurexin family, Neurexin IV (NRX), which is localized to septate junctions (SJs) of epithelial and glial cells. NRX is a transmembrane protein with a cytoplasmic domain homologous to glycophorin C, a protein required for anchoring protein 4.1 in the red blood cell. Absence of NRX results in mislocalization of Coracle, a Drosophila protein 4.1 homolog, at SJs and causes dorsal closure defects similar to those observed in coracle mutants. nrx mutant embryos are paralyzed, and electrophysiological studies indicate that the lack of NRX in glial-glial SJs causes a breakdown of the blood-brain barrier. Electron microscopy demonstrates that nrx mutants lack the ladder-like intercellular septa characteristic of pleated SJs (pSJs). These studies identify NRX as the first transmembrane protein of SJ and demonstrate a requirement for NRX in the formation of septate-junction septa and intercellular barriers.

MeSH Terms:
- Amino Acid Sequence
- Animal
- Blood Cells
- Blotting, Northern
- Blotting, Western
- Cloning, Molecular
- Drosophila/embryology*
- DNA Mutational Analysis
- Electrophysiology
- Epithelium/physiology
- Genetic Markers
- Membrane Proteins/genetics*
- Microscopy, Electron
- Molecular Sequence Data
- Nerve Tissue Proteins/genetics*
- Nervous System/physiology
- Nervous System/embryology
- Nervous System/chemistry
- Nervous System Physiology
- Neuroglia/physiology
- Neurons/physiology
- Sequence Analysis, DNA
- Support, Non-U.S. Gov't
- Support, U.S. Gov't, P.H.S.
- Tight Junctions/ultrastructure
- Tight Junctions/physiology
- Tight Junctions/chemistry*

Substances:
- Nerve Tissue Proteins
- Membrane Proteins
- Genetic Markers
- neurexin IV

Secondary source id:
- GENBANK/U18017
- GENBANK/Z42448
- GENBANK/U17905
- GENBANK/U18000
- GENBANK/T27170

- GENBANK/X86685

Grant support:
- HD09948/HD/NICHD

PMID: 8978610, UI: 97133213

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Revised: January 10, 2000.