

VaProS チュートリアル

インスリン受容体のリガンド結合と病気に関連する残基を調べる

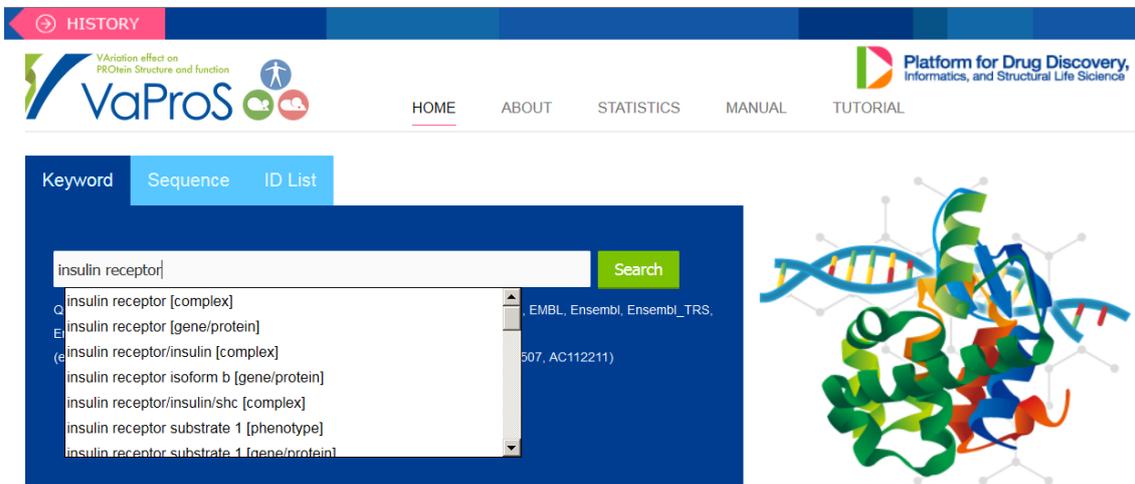
概要

2013年に、インスリン-インスリン受容体複合体の結晶構造が報告されました (JG Menting et al. Nature 493, 241-245 (2013) doi:10.1038/nature11781)。この複合体構造を利用して、リガンド結合に参与するアミノ酸残基および糖尿病との関連が示されているアミノ酸残基について調べます。

解説

“insulin receptor”で keyword サーチすることからはじめます。

VaProS トップ画面 (<http://p4d-info.nig.ac.jp/vapro/>) にアクセスします。その後、Keyword の検索窓に insulin receptor と入力し、Search ボタンをクリックします。



The screenshot shows the VaProS web interface. At the top, there is a navigation bar with a 'HISTORY' button and the VaProS logo. Below the logo, there are navigation links for HOME, ABOUT, STATISTICS, MANUAL, and TUTORIAL. The main content area has three tabs: 'Keyword', 'Sequence', and 'ID List'. The 'Keyword' tab is active, and a search box contains the text 'insulin receptor'. A green 'Search' button is to the right of the search box. Below the search box, a dropdown menu lists search results:

- insulin receptor [complex]
- insulin receptor [gene/protein]
- insulin receptor/insulin [complex]
- insulin receptor isoform b [gene/protein]
- insulin receptor/insulin/shc [complex]
- insulin receptor substrate 1 [phenotype]
- insulin receptor substrate 1 [gene/protein]

To the right of the search results, there is a 3D ribbon diagram of a protein structure, likely the insulin receptor, shown in various colors (green, blue, red, orange).

insulin receptor に関連するヒト、マウス、ラットのタンパク質や遺伝子の情報が出力されます。興味のある INSR, insulin receptor, Homo Sapiens の行にチェックを入れて、Details (Go) ボタンをクリックします。

Query: "insulin receptor"

Hits	
Gene/Protein	130
Ligand	0
Phenotype	3

Gene/Protein results - hits: 130

Details (Go)

Filtered by:

Type: molecule type Organism: organism TrEMBL: TrEMBL

x Homo sapiens

ID	Type	Name	Full Name	Organism	EntraGene ID	UniProtKB	TrEMBL	Molecule Interactions	PPV	3D Interactions	NLDR
1	[synonym] Insulin-like growth factor 1 receptor	IGF1R	Insulin-like growth factor 1 r...	Homo sapiens	3480	P08089	none	1257	123	1	1
2	[synonym] Insulin receptor	INSR	Insulin receptor	Homo sapiens	3543	P06213	none	710	128	1	1
3	[synonym] Insulin receptor-related p...	INSRR	Insulin receptor-related protein	Homo sapiens	3545	P14616	none	227	3	1	1
4	[synonym] Insulin receptor substrate...	IRS4	Insulin receptor substrate 4	Homo sapiens	8471	Q14654	none	155	155	1	0
5	[synonym] Insulin receptor substrate...	EAIAP2	Brain-specific angiogenesis in...	Homo sapiens	10458	Q9J0B8	none	111	111	1	0
6	[synonym] Insulin receptor substrate...	IRS1	Insulin receptor substrate 1	Homo sapiens	3567	P35565	none	105	104	1	0
7	[synonym] Insulin receptor-binding p...	GBB10	Growth factor receptor-bound p...	Homo sapiens	2887	Q13322	none	60	80	1	0
8	[synonym] Insulin receptor substrate...	IRS2	Insulin receptor substrate 2	Homo sapiens	8960	Q9Y4H2	none	59	59	1	0
9	[synonym] Insulin-like growth factor II receptor	IGF2R	Cation-independent mannose 6 p...	Homo sapiens	3482	P11717	none	50	45	1	0
10	[synonym] Insulin receptor substrate...	DOK4	Docking protein 4	Homo sapiens	55715	Q8ILEW6	none	38	38	1	0
11	[synonym] Insulin receptor tyrosine...	EAIAP2L1	Brain-specific angiogenesis in...	Homo sapiens	55071	Q9J0B4	none	33	33	1	0
12	[synonym] Insulin receptor substrate...	DOK5	Docking protein 5	Homo sapiens	55816	Q9P104	none	20	20	1	0

その操作により VaProS 内の DB・ツールに遷移します。下図の左のアイコンの並びの中の 3D Interaction をクリックするとその右側の領域に 3D Interaction ウィンドウが現れます。そのウィンドウの一番左上にあるボタンを押すとウィンドウサイズが大きくなり見やすくなります。

3D Interaction: Contact Bar(summary)[0.0 %]

seq.id(%): [0] [30] [40] [50] [60] [70] [80] [90] [95] [100] [show] [download]

PID	QueryLength	Homologous Sequence in PDB	UniProt Query	TITLE
13072	1382	500	INSR HUMAN(P06213)	RecName: Full=Insulin recep RecName: Full=Insulin recep submit beta:Flags: Precurs

QUERYSEQ
 MNTDPRGMAAPLLVAVAAALLGAGHLVPEVYVPMIDIRNILLHELHENSSTEGHLDLILMRTPREDFRQLSFRLLT
 ELCYLATIDSRILDSVEDNYLVNKKDNEECDDICPGTAKGTNCPATVINGGFVERKWTSHOCKVCPITCKSHOCTAEG
 CHQYVHHNNCIPCEPSGYTIMNSNLLCTPOLGPCPKVCHLLEGBITIDSVTSAGELRQCTVINGSLIINIRGGNNLAELE
 GKLFHHNPKLCLSEIHMEEVSGTRGRIERNDIAKTKNDQASDENLLKFSYIRTSFDKILLRWEPPHPIRHLIGML
 CERITYSASDIIYVOTDITPVSFLDPISYKNSSQIILKMPSPDPNINITHLVNFKEDGDELFELDYDLKGLVPS
 CAEDPAPSRKRRSLGVGVNVTAVPTVAFPNTSSISVPTSPCEHRRFEDVYVKNLSLVISQLRHFYRTELQACNDTPRE
 SRKHFALEGRQLRGLSPGNYSVRIRATSLAINGSWTEPTFYVYTDVLDVPSNIAKTIIGPLIFVFLFSVIGSYLFLRKR
 ETRYAVKTMESASLRERIEFLNEASWNGFTHHWYRLLGVYSGUPTLVNMLMAHQDLSYLSLRFPEADNPGRPPT
 PIMAFESLIDGHTTSSCMWFDVLEITLQLACDPIYQGLSNEGLHFMDSGYLDPNDQPERVTLMMCMQFAPKMPPT
 FKRSYEEHLPYTHMNGKNGRILTLPSNPS

[BLAST file for PDB] [plain] [bar] [BLAST for UniProt: [plain] [bar] [multiple alignment] [PSSM file]]

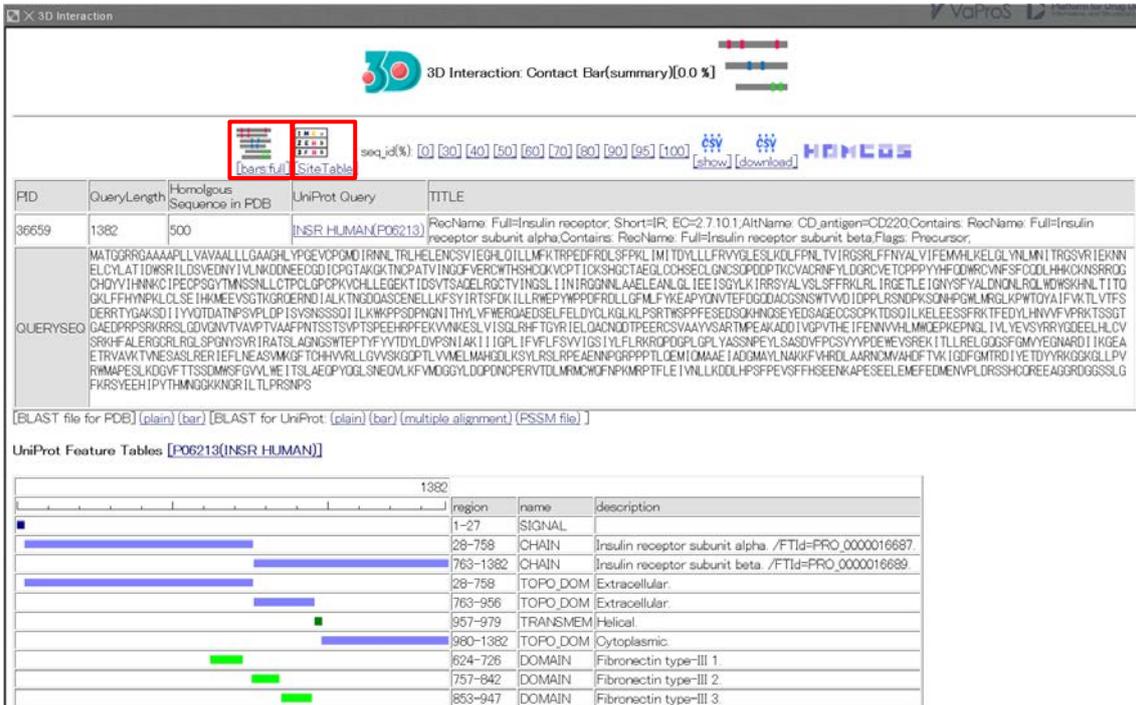
UniProt Feature Tables [P06213(INSR HUMAN)]

region	name
1-27	SIGNAL
28-758	CHAIN

20 protein INSR Homo sapiens protein PTPN1

以下、ウインドウサイズを最大化した 3D Interaction ウィンドウです。

insulin receptor (INSR)にアミノ酸配列が類似のタンパク質で Protein Data Bank (PDB)に立体構造が登録されているものが、MONOMER の表に表示されます。初期状態では、似たホモログは代表だけが表示されます (summary)。すべての立体構造の一覧を見るために [bars (full)] をクリックします。



3D Interaction: Contact Bar(summary)[0.0 %]

seq_id(%) [0] [30] [40] [50] [60] [70] [80] [90] [95] [100] [show](#) [download](#) [show](#) [download](#) [show](#) [download](#)

PID	Query Length	Homologous Sequence in PDB	UniProt Query	TITLE
36659	1382	500	[INSR_HUMAN(P06213)]	RecName: Full=Insulin receptor; Short=IR; EC=2.7.10.1; AltName: CD_antigen=CD220; Contains: RecName: Full=Insulin receptor subunit alpha; Contains: RecName: Full=Insulin receptor subunit beta; Flags: Precursor;

MATGRRGAAAPLLVAVAAALLGAAGHLYPEVCPGMDIRNNLTRLHELENCVIEGHLQILLMFKTRPEDFRDLSPFKLIMITDYLLFRVYGLSKDLFPNLTVIRGSRLLFFNYALVIFEMHLKELGLNLMNIIRGSRVIRKNN
 ELCYLATIDWSRILDSVEDNYIVLNKDDNEEGDIPCGTAKGKTNCPATVINGOFVERCWTSHDQKVCPTICKSHGCTAEGLCDHSECLGNCSDDPDTKCAQRNFYLDGRVETCPPPYHFDWACVNFSPDOLHKKCKNSRROG
 CHQYVHNKNCIPECPGGYTMSSNLLCTPLGLCPKVCYHLEGEKTIQSVTSAGELRGCTVINGSLIINIRGGNLAELANLGLIEEISGLYKIRRSYALVSLSPFRKLRLLRGETLEIGNYSFYALDNQNLROLWWSKHNLITITD
 GKLFHFNKPLDSEIHAMEEYSGTGRDGRNDIALKTNQDQASCEHELLKFSYIRTSFDKILLRWEPYYPDFRDLGLMFLYKAPYQNVTEFDGDDAGDSNSWTVDIDPPLRSNDPKSONHFGMLMRGLKFWTOYVAFVKTLVFS
 DERRTYGAASDIIYYOTDANTSPFLQPIYSVNSSSDILKRWPPDPNGNITHLYVFERQAEDELFDYGLKLRPSTHSPFSESDSKHNGEYEDSAGEDSCPITDSDILKEEESFRKTFEDLHVVYFPRKTSSTG
 QAEIPSPSRKRSLLGDVQNTVAVPTVAFFNTSSIVPTSPFEEHFEKWKVESLVSLLRHFVDRVELDQNDQDPEERSVAAYVSARITMPEAKADQIVSPVTHEIFENNVALLMDEKPEKQNLIVLVEYSYVQDELHLQV
 SRKHFALERQRLRLSPQNYSVIRIATSLAGNSWTEPTFYFYVDLQVPSNIAKIIIGPLIFVFLFSVITDSIYVFLRKRQDFGLPLVASSNPEYLSASQVFPSCSYYPDEWEYSREKILLRELQDSFQGMVEGNARDIIKGEA
 ETRVAVKTVMSASLRERIEFLNEASVMKGFQCHVRLGLVSKGQPTLVAMELMAHGDLKSYRLSRPEAENPGRPPPTLGEITQMAAEIADGMALNAKGFVHRDLAARNMVAHDFVWIGDFMTRDIVEIDYRKGKGLLPV
 RHMAFESLKDGVFTTSSQIMKFGVYVMEITSLAEPYDGLSNEQVLFVMDGGYLDQPNQPERVYDLMRMQWQFNKMPPTFLEIVNLLKDDLHSPFPEVSVFFHSEENKAPSEEELEMEFEDMENVFLDRSSHQDREAGSDGSSSLG
 FKRSYEEHIVYTHMNGKKNRILLTPRSNPS

[BLAST file for PDB] [plain] [bar] [BLAST for UniProt] [plain] [bar] [multiple alignment] [PSSM file]

UniProt Feature Tables [P06213(INSR_HUMAN)]

region	name	description
1-27	SIGNAL	
28-758	CHAIN	Insulin receptor subunit alpha. /FTid=PRO_0000016687.
763-1382	CHAIN	Insulin receptor subunit beta. /FTid=PRO_0000016689.
28-758	TOPO_DOM	Extracellular.
763-956	TOPO_DOM	Extracellular.
957-979	TRANSMEM	Helical.
980-1382	TOPO_DOM	Cytoplasmic.
624-726	DOMAIN	Fibronectin type-III 1.
757-842	DOMAIN	Fibronectin type-III 2.
853-947	DOMAIN	Fibronectin type-III 3.

下方にスクロールすると MONOMER の表が現れます。この表をみると、インスリン受容体の細胞外リガンド結合ドメイン(バーが左寄りのもの)についていくつかの長さの結晶構造が解かれていること、また細胞内チロシンキナーゼドメインの結晶構造も複数報告されていることが分かります。

PDB id: 3w14 が目的のインスリン-インスリン受容体(細胞外ドメイン)複合体構造です。chains E と F がホモ 2 量体を形成していますが、インスリン(chains A と B)認識の仕方は chains E と F で異なります。まず 3w14 E をクリックします。

3D interaction のトップ画面に戻り[Site Table]をクリックして、各アミノ酸残基に関する情報を表示させます(下図参照)。各アミノ酸残基について、左から、残基番号、アミノ酸の種類、二次構造情報、溶媒露出度、PDB 登録情報、類似タンパク質における置換例が書かれています。また、contact mols にはその残基への結合が見られた化合物の情報が、feature table にはその残基の機能が、variant にはその残基に見られる点変異例とが書かれています。この点変異が病気に関連している場合はそのことも書かれています。

contact mols から、R41 と N42 がインスリン A 鎖の認識に、N42, F66, K67, F91, R92, E124 がインスリン B 鎖の認識に関わっていることが分かりました。

variant からインスリン受容体全体で、45 残基の点変異が病気と関連付けられており、そのうち 28 残基が細胞外ドメインに、17 残基が細胞内ドメインにあることが分かりました。例として、SITE 42 をクリックしてみます。

3D Interaction: Site Table[0.0 %]

1 M e e
2 E H b
3 F H b

[seq_id\(%\)](#) [0] [30] [40] [50] [60] [70] [80] [90] [95] [100]
 [CSV](#) [CSV](#) [HTML](#)

[\[bars summary\]](#) [\[bars full\]](#)

PID	QueryLength	Homologous Sequence in PDB	UniProt Query	TITLE
9005	1382	500	INSR HUMAN(P06213)	RecName: Full=Insulin receptor; Short=IR; EC=2.7.10.1;AltName: CD_antigen=CD220;Contains: RecName: Full=Insulin receptor subunit alpha;Contains: RecName: Full=Insulin receptor subunit beta;Flags: Precursor.

[\[BLAST file for PDB\]](#) [\[plain\]](#) [\[bar\]](#) [\[BLAST for UniProt\]](#) [\[plain\]](#) [\[bar\]](#) [\[multiple alignment\]](#) [\[FSSM file\]](#)

[n]:site number of query sequence. [a]:amino acid of query sequence. [s]:predicted secondary structure.
 [e]:predicted exposed/buried. [acc]:predicted accessibility. [pdb]:PDB code of homologous structure.
 [contact mols]:binding other molecules [observed aa]:Observed amino acids among homologous sequences. [feature table]:UniProt Feature Table
 [variant]:UniProt Human Variant.

n	a	s	e	acc	pdb	contact mols	observed aa	feature table	variant
SITE 1	M	-	-	-	-		M	SIGNAL	
SITE 2	A	-	-	-	-		AG	SIGNAL	A>G:Polymorphism
SITE 3	T	-	-	-	-		ST	SIGNAL	
SITE 4	G	-	-	-	-		G	SIGNAL	
SITE 5	G	-	-	-	-		GR	SIGNAL	
SITE 40	I	e	b	0.0	31oh E		IMASVNLDFEGKPORTY	TOPO_DOM Extracellular.	
SITE 41	R	e	b	48.6	331oh E	hetero INSR RAT IGF1 HUMAN INSR BOVIN INSR HUMAN INSR HUMAN homo precipitant	RKQEDLAFGINPSTVY	TOPO_DOM Extracellular.	
SITE 42	N	s	e	55.2	331oh E	hetero INSR HUMAN INSR RAT IGF1 HUMAN INSR BOVIN compound [142] homo	NLSM	TOPO_DOM Extracellular.	N>K:Disease
SITE 43	K	e	b	60.2	331oh E	homologous MAF	RSKDENGMT	CARBOHYD N-linked (GlcNAc...), TOPO_DOM	
SITE 44	M	e	b	U.0	331oh E			IUPU_DOM extracellular.	
SITE 46	F	e	b	48.8	331oh E	hetero INSR RAT IGF1 HUMAN INSR BOVIN INSR HUMAN homo precipitant	FPDSGLKNAEIRTV	SITE Insulin-binding. TOPO_DOM Extracellular.	
SITE 67	K	s	e	72.6	331oh E	hetero IGF1 HUMAN INSR BOVIN INSR HUMAN	KTARHVDVEFNGILPSV	TOPO_DOM Extracellular.	
SITE 69	T	e	b	2.2	331oh E		NATYGHLS	mpn nru Extracellular.	
SITE 90	L	e	b	1.7	331oh E			IUPU_DOM Extracellular.	
SITE 91	F	e	b	23.4	331oh E	hetero INSR RAT INSR HUMAN INSR HUMAN INSR BOVIN homo precipitant	FYIVASKEGL	TOPO_DOM Extracellular.	
SITE 92	R	e	b	29.6	331oh E	hetero IGF1 HUMAN INSR BOVIN INSR HUMAN homo precipitant	RAELHSGV	TOPO_DOM Extracellular.	
SITE 93	M	e	b	2.0	331oh E		MLAIDTMHDEFGNERS	mpn nru Extracellular.	

SITE	124	E	S	22.1	3loh	Ehetero	INS_HUMAN	INSR_HUMAN	homo	precipitant	ESDWRTL	TOPO_DOM	Extracellular.
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インスリン受容体(PDB id: 3w14)の chain E の N(アスパラギン)42 に関する情報をまとめたページです。Rabson-Mendenhall syndrome(インスリン受容体異常症の一種で、高度のインスリン抵抗性を呈す)の患者では、このアミノ酸残基が K(リジン)に置換されていることが分かります。3D Complex Information に示された情報から、このアミノ酸残基は、 $\alpha 2\beta 2$ ヘテロ 4 量体構造をもつインスリン受容体の細胞外ドメイン(α)のホモ 2 量体化に寄与するとともに、リガンドであるインスリンの A 鎖にも B 鎖にも結合する重要なアミノ酸残基であることがわかります。このため、N42→K の点変異により、インスリン受容体の立体構造やリガンド認識に異常が生じた可能性が高いと考えられます。同様に、他のアミノ酸残基の重要性も調べることができます。

SITE Summary for the 42-nd Site(N)

PID	QueryLength	FocusSite	TITLE
9005	1382	42 N	RecName: Full=Insulin receptor; Short=IR; EC=2.7.10.1; AltName: CD_antigen=CD220; Contains: RecName: Full=Insulin receptor subunit alpha; Contains: RecName: Full=Insulin receptor subunit beta; Flags: Precursor;

UniProt Information

AC/ID	AC:F06213 ID:INSR_HUMAN
Feature Table for 42-th site	VARIANT: N -> K (in RMS; impairs transport to the plasma membrane and reduces the affinity to bind insulin). [ECO:0000269 PubMed:2121734, ECO:0000269 PubMed:2365819]. /FTId=VAR_004079. STRAND: [ECO:0000244 PDB:2HR7]. COMBIAS: Leu-rich. CHAIN: Insulin receptor subunit alpha. /FTId=PRO_0000016687. TOPO_DOM: Extracellular. [ECO:0000305].
VARIANT for 42-th site	N->K Disease dbSNP : Rabson-Mendenhall syndrome (RMS) [MIM:262190]

Evolutionary Information

Percentage of Amino Acids in Homologous Protein
N:58% L:23% S:14% M:5%

3D Structure Information

Template For Monomer	predicted SecStr	predicted ExpBur	Predicted Relative Acc(%)
3loh	S (<i>bend</i>)	e (<i>exposed</i>)	55.2

3D Complex Information

Predicted Bind Molecules
hetero:22 homo:1 compound :1
Templates for 3D complexes
hetero [42984:INSR RAT] 4xst A 6 B 6 4xst A 5 B 5 4xst A 4 B 4 4xst A 2 B 2 4xst A 3 B 3 4xst A 1 B 1 [32325:INS HUMAN] 3w13 A 1 E 1 3w11 E 1 B 1 [10543:IGF1 HUMAN] 4xss B 4 A 4 4xss B 6 A 6 4xss B 5 A 5 4xss B 2 A 2 4xss B 1 A 1 4xss B 3 A 3 [2251:INS HUMAN] 4oga E 1 B 1 [3730:INS BOVIN] 3w14 F 1 G 1 3w14 F 2 G 2 3w12 A 1 D 1 3w11 E 1 A 1 3w14 E 2 A 2 3w14 E 1 A 1 3w13 A 1 D 1 homo [11321:INSR HUMAN] 2hr7 A 1 B 1 compound [NAG] 2hr7 A 1 C 1

3D Interaction タブから Phenotype タブに移動すると、このタンパク質が関与している疾患が表示されます。Reference の OMIM をクリックすると、ヒトの遺伝子と遺伝病のオンラインカタログである OMIM (Online Mendelian Inheritance in Man) のページが開き、その疾患に関する説明を読むことができます。

The screenshot shows a web application interface with a sidebar on the left containing various database icons: COXPRESdb, Pathway DB, Phenotype (highlighted with a red box), S-VAR, S-VAR, Autophagy DB, and Genome Explorer. The main content area is titled 'Phenotype' and contains a table with the following data:

Molecule	Disease	Reference
INSR P06213	DIABETES MELLITUS, INSULIN-RESISTANT, WITH ACANTHOSIS NIGRICANS	OMIM
	DIABETES MELLITUS, NONINSULIN-DEPENDENT	OMIM
	DONOHUE SYNDROME	OMIM
	HYPERINSULINEMIC HYPOGLYCEMIA, FAMILIAL, 5	OMIM
	PINEAL HYPERPLASIA, INSULIN-RESISTANT DIABETES MELLITUS, AND SOMATIC ABNORMALITIES	OMIM

A blue arrow points from the 'OMIM' reference in the first row to a detailed OMIM entry page. The OMIM entry page is also highlighted with a red box and contains the following information:

Table of Contents for 4610549

DIABETES MELLITUS, INSULIN-RESISTANT, WITH ACANTHOSIS NIGRICANS

Alternative titles (synonyms):
 INSULIN RECEPTOR DEFECT DC WITH INSULIN-RESISTANT DIABETES MELLITUS AND ACANTHOSIS NIGRICANS
 DIABETES MELLITUS, INSULIN-RESISTANT WITH ACANTHOSIS NIGRICANS, TYPE A
 IRAN, TYPE A

Phenotype-Genes Relationships

Gene	Phenotype	Inheritance	Frequency	Gene Name	OMIM
INSR	Diabetes mellitus, insulin-resistant, with acanthosis nigricans	AD	?	INSR	4610549

TEXT
 A number sign (#) is used with this entry because insulin-resistant diabetes mellitus with acanthosis nigricans can be caused by heterozygous, homozygous, or compound heterozygous mutation in the INSR gene (142970) on chromosome 17q11.

Clinical Features
 Kaplan et al. (1974) described the syndrome of insulin resistance and acanthosis nigricans (type A), a syndrome of teenage females with signs of insulin resistance and accelerated growth in whom a defect in cell receptors for insulin may be present; and type B, a syndrome in older females with signs of an autoimmune disease in whom circulating antibodies to the insulin receptor are found. Although not identical cases (see text), their assumption that all these patients and those in the literature were insulin-resistant was based, although the syndrome has been observed in presence of Acanthosis Nigricans, Indian, Vietnamese, and Japanese origin. Despite genetic heterogeneity, inheritance is rare. Families with the type A syndrome have polydystrophic ovaries. (PMID: 142970)

Rodgers et al. (1980) described 3 pts with adult diabetes in combination with acanthosis nigricans and minor physical abnormalities: bilateral narrowing of the skull, proclivity of body fat, acral hyperkeratosis (enlarged ears, nose, chin, and finger tips), brachydactyly, proclivity of the eye globes, and dental anomalies (impacted lower teeth, narrow and premature caries, abnormally positioned lower incisors and upper incisors). Fasting plasma insulin was 200 times normal, insulin-binding was defective, and standard analysis showed a normal number of insulin-binding sites per cell but a complete lack of insulin binding to the high-affinity receptor component. (PMID: 736888)

In patients with an inherited antibody defect of the insulin receptor, Rodgers et al. (1980) found that stimulation of glucose uptake, an early effect of insulin, was normal, but insulin-mediated stimulation of DNA synthesis, a late effect, was defective. Both the antibody defect and the deficient stimulation of DNA synthesis were apparent at low concentrations of insulin only and disappeared at very high concentrations. (PMID: 736888)

Mason et al. (1982) described a 3-year-old girl with acanthosis nigricans, insulin-resistant diabetes mellitus, hyperkalemia, proptosis, macrognathia, and large ears. Generalized hypertrichosis and hyperosty of the distal tibia were present. A decrease in the number of insulin receptors was demonstrated. In the patient reported by Lavenex et al. (1982), polydystrophic ovaries were also present. Insulin resistance with acanthosis nigricans but with normal receptors may have a postreceptor defect (Bor et al. 1978). Pines et al. (1986) studied a 10-year-old black female with abnormal morphology, acral hyperkeratosis, and acanthosis nigricans that was first noted at age 4 years. Insulin receptor-receptor (R1/R2) ratio was decreased and the remaining receptor showed a functional impairment. Perhaps one should speak of types A1 and A2 of insulin resistance and acanthosis nigricans (IRASN), type A2 being a form with a postreceptor defect. (PMID: 3601444)

Chattopadhyay et al. (1984) and Chattopadhyay et al. (1985) described patients with type A insulin resistance and abnormal insulin receptor kinase activity. In 2 patients with type A insulin resistance,

上記の検索により、insulin receptor について約 10 分で、以下の情報を得ることができました。

- 現時点での Protein Data Bank への立体構造登録状況 (長さの異なる細胞外ドメインの構造数種と、細胞内チロシンキナーゼドメインの構造が多数登録されていること)
- リガンド認識残基の情報 (R41 と N42 の 2 残基がインスリン A 鎖の認識に、N42, F66, K67, F91, R92, E124 の 6 残基がインスリン B 鎖の認識に関わること)
- 点変異と疾患との関連 (45 残基の点変異が疾患と関連付けられている。このうち 28 残基は細胞外ドメイン、17 残基は細胞内ドメインに位置すること)

以上