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Software and database for the analysis of mutations in the human WT1 gene

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ABSTRACT

The WT1 gene, located at 11p13, encodes a zinc finger transcription factor involved in renal and gonadal development and in Wilms' tumor. Constitutional mutations of this gene have been described in most patients with Denys Drash syndrome (mesangial sclerosis associated with male pseudohermaphrodism and/or Wilms' tumor), but also in patients with genitourinary abnormalities and Wilms' tumor (WT) or presenting with only unilateral or bilateral WT. Moreover, ~10% of Wilms' tumors carry WT1 mutations at the somatic level. To facilitate the genotype–phenotype correlation analyses, we have created a software package along with a computerized database of germline (70 entries) and somatic (28 entries) mutations reported in the literature.

INTRODUCTION

WT1 is a zinc finger transcription factor mainly expressed during renal and gonadal development (1). It is encoded by a 50 kb long gene containing 10 exons and located at 11p13. Exons 1–6 encode a proline/glutamine rich transcriptional regulation region. Different functional domains involved either in repression or in activation of transcription (2,3) and a region involved in homodimerisation of the protein (4) have been characterized. Exons 7–10 encode the four zinc fingers of the DNA-binding domain. Two alternative splicing regions, one corresponding to the 17 amino acids encoded by exon 5 and the other one corresponding to amino acids KTS encoded by the 3′ end of exon 9, allow synthesis of four isoforms, with definite proportions (5), different binding specificity (6,7) and different subnuclear localization (8). All these data underlie a complex mechanism of transcriptional regulation by WT1. Although transient transfection assays have shown that WT1 may regulate transcription of several genes, including IGF2 (9), PDGFA (10) and WT1 (11), the physiological and functional significance of these target genes is still unknown.

Constitutional deletion of one copy of the WT1 gene is responsible for predisposition to Wilms' tumor (WT) and for genitourinary abnormalities observed in patients with WAGR syndrome (WT, aniridia, genitourinary abnormalities, and mental retardation due to deletion of band 11p13). Constitutional heterozygous intragenic mutations have been described in: (i) most patients with Denys Drash syndrome (DDS) (mesangial sclerosis associated with male pseudohermaphrodism and/or WT); (ii) some patients with genitourinary abnormalities and WT; (iii) some patients presenting with only unilateral or bilateral WT, among which a familial case (as a review see 12). Most of the mutations in the DDS patients are missense mutations occurring in exon 9, or less frequently in exon 8, and affecting the DNA-binding capacity of WT1 (13), whereas mutations described in the other categories of patients preferentially involve the proximal part of the gene and lead to truncated proteins. At the somatic level, ~10% of Wilms' tumors carry WT1 mutations, with a majority of stop and frameshift mutations. Different groups reported analyses of correlations between genotype and phenotype (12,14,15). However, analyses of such complex information would be greatly facilitated by the development of a computerized tool, all the more because accumulation of data is necessary to reach statistically-significant correlations.

DATABASE AND SOFTWARE

In an effort to standardize the information regarding WT1 mutations and to analyse genotype–phenotype correlations, we developed a computerized database using software already used for other genes (16–18). For each mutation, information was provided at several levels: at the gene level (exon and codon number, wild type and mutant codon, mutational event, type of mutation), at the protein level (wild type and mutant amino acid) and at the clinical level, for the different symptoms developed by patients with WT1 germline mutations (presence or absence of nephropathy, karyotype, external genitalia and internal reproductive organs, presence of unilateral or bilateral WT or nephrectomy). Data concerning research of the mutation in the parents were also provided. For somatic WT1 mutations, data concerning the age of diagnosis of the tumor, the presence of associated clinical features and the karyotype or sex of the patient were provided. All point mutations, insertions or deletions lying in the coding sequence were registred. Amino acid changes and generation of stop codons following frameshift mutations were automatically determined by the software. Major rearrangements, as well as mutations in introns, were omitted as they cannot be accomodated in the present version of the software.

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File #	Exon	Base	Codon	wt codon	Mutant codon	Event	Type	CpG	Name	wt AA	Mutant AA	Cancer	Origin	LOH	external genitalia	internal reproductive organs	karyotype	mutation in parents	nephrectomy	nephropathy	other	Ref
115	1	28	10	GCG	del29a	Stop at 120	Fr.		9464	Ala	Fr.	bil WT	Germ	yes	male					no nephropathy	WT at 3 mo	39
65	1	85	29	AGC	ins5c	Stop at 130	Fr.		186523	Ser	Fr.	unil WT	Germ	yes	cryptorchidism		46, XY			no nephropathy (18 mo)	horseshoe kidney	36
116	1	367	123	GGC	del26a	Stop at 170	Fr.		9200	Gly	Fr.	bil WT	Germ	yes	female					no nephropathy	WT at 15 mo	39
117	1	409	137	TGC	del7a	Stop at 215	Fr.		9184	Cys	Fr.	unil WT	Germ	yes	male	testicular aplasia				no nephropathy	WT at 12 mo	39
118	2	541	181	CCC	TCC	C->T	Ts	No	9094	Pro	Ser	unil WT	Germ	no	female					no nephropathy	WT at 30 mo	39
32	3	663	221	TAC	TAG	C>G	Tv	No	CN	Tyr	Stop	bil WT	Germ		cryptorchidism					compatible with MS		19
42	4	670	224	GAC	del17a	Stop at 228	Fr.		RG	Asp	Fr.	bil WT	Germ	yes	cryptorchidism/hypospadias		46, XY			no nephropathy		37
119	5	758	253	GCG	GCG	G->C	Tv	No	9614	Gly	Ala	unil WT	Germ	no	female					no nephropathy	WT at 29 mo	39
99	6	813	271	TAC	TAG	C>G	Tv	No	WT 10	Tyr	Stop	bil WT	Germ	yes	cryptorchidism	Sertoli-only gonads		no (F) / ND (M)		no nephropathy (8 y)		38
30	6	820	274	GAT	ins1b	Stop at 275	Fr.		PM/3/GOS389	Asp	Fr.	bil WT	Germ		ambiguous	atrophy	46, XY	no (F) / no (M)	(2.1 y)	MS		20
33	6	826	276	CAC	del1b	Stop at 306	Fr.		SL	His	Fr.	unil WT	Germ		female	ovaries	46, XX			nephrotic syndrome at 15 y		19
43	6	874	292	GGT	del1a	Stop at 306	Fr.		TS	Gly	Fr.	unil WT	Germ	yes	cryptorchidism/hypospadias			yes (F with WT)		no nephropathy (3 y)		37
121	7	901	301	CGA	TGA	C->T	Ts	Yes	HDWT7	Arg	Stop	bil WT	Germ		female					no nephropathy	WT at 18 mo, twin of HDWT6	39
120	7	901	301	CGA	TGA	C->T	Ts	Yes	HDWT6	Arg	Stop	unil WT	Germ		female					no nephropathy	WT at 19 mo, twin of HDWT7	39
123	7	938	313	TCG	TAG	C->A	Tv	No	9561	Ser	Stop	unil WT	Germ	no	male					no nephropathy	WT at 34 mo	39
122	7	938	313	TCG	TAG	C->A	Tv	No	9318	Ser	Stop	bil WT	Germ	yes	female					no nephropathy	WT at 7 mo	39
29	7	989	330	TGC	TAC	G->A	Ts	No	KJ	Cys	Tyr	NR	Germ		female (mild clitoromegaly)		46, XX			MS		21
10	8	1064	355	TGT	TAT	G->A	Ts	No	KS / 1614	Cys	Tyr	unil WT	Germ		female	ovaries	46, XX	no (M) / ND (F)		nephropathy	homozygous mutation	22
101	8	1079	360	TGT	TAT	G->A	Ts	No	R6	Cys	Tyr	no WT	Germ		ambiguous	testes	46, XY			MS	death at 6 mo	23
39	8	1078	360	TGT	GGT	T->G	Tv	No	3	Cys	Gly	unil WT	Germ	no	female			no (F) / ND (M)		nephropathy		24
66	8	1084	362	CGA	TGA	C->T	Ts	Yes	Z-2368	Arg	Stop	fam WT	Germ	yes	female			yes (asymptomatic F)		no nephropathy (8 mo)	2 sisters with Wilms' tumor	40
40	8	1084	362	CGA	TGA	C->T	Ts	Yes	4	Arg	Stop	bil WT	Germ	yes	ambiguous	testes	46, XY			MS		24
35	8	1084	362	CGA	TGA	C->T	Ts	Yes	WIT29	Arg	Stop	unil WT	Germ		female			no (F) / no (M)		no nephropathy (11 mo)		41
108	8	1097	366	CGT	CAT	G->A	Ts	Yes		Arg	His	no WT	Germ		female		46, XY			MS	diaphragmatic hernia	25
106	8	1097	366	CGT	CAT	G->A	Ts	Yes		Arg	His	no WT	Germ		female	dysgenic	46, XY			compatible with MS	bicornuated uterus	26
19	8	1097	366	CGT	CAT	G->A	Ts	Yes	SV	Arg	His	no WT	Germ		female	streak/dysgenic testis	46, XY			MS	gonadoblastoma	27
7	8	1097	366	CGT	CAT	G->A	Ts	Yes	LVH/GOS456	Arg	His	unil WT	Germ		ambiguous		46, XY	no (F) / no (M)	(9 mo)	nephropathy		20
63	8	1119	373	CAC	CAA	C->A	Tv	No	WT5100	His	Gln	bil WT	Germ		female	gonadoblastoma / streak	46, XY			nephropathy	bicornuated uterus	28
41	8	1119	373	CAC	CAG	C>G	Tv	No	5	His	Gln	no WT	Germ		hypospadias		46, XY	no (F) / no (M)		nephropathy		24
54	8	1129	377	CAT	TAT	C->T	Ts	No	D10	His	Tyr	no WT	Germ		female	streak gonads	46, XY	no (F) / no (M)	(19 mo)	nephropathy		29
12	8	1130	377	CAT	CGT	A->G	Ts	No	D1	His	Arg	unil WT	Germ	yes	ambiguous		46, XY	no (F) / no (M)		MS	mutation on paternal allele	30
34	9	1156	386	AAA	ins1c	Stop at 408	Fr.			Lys	Fr.	no WT	Germ		cryptorchidism/hypospadias			no (F) / no (M)		nephropathy		31
124	9	1168	390	CGA	TGA	C->T	Ts	Yes	HDWT8	Arg	Stop	unil WT	Germ		maldescended testes					proteinuria	WT at 24 mo	39
36	9	1168	390	CGA	TGA	C->T	Ts	Yes	NP57/NP58	Arg	Stop	bil WT	Germ	yes	normal external phenotype			no (F) / ND (M)		no nephropathy (11 mo)		42
9	9	1180	394	CGG	TGG	C->T	Ts	Yes	MM / 1560	Arg	Trp	unil WT	Germ		female	ovaries	46, XX	no (F) / no (M)		nephropathy		22
109	9	1180	394	CGG	TGG	C->T	Ts	Yes	AK	Arg	Trp	no WT	Germ		female		46, XY			MS		32
107	9	1180	394	CGG	TGG	C->T	Ts	Yes	A1	Arg	Trp	unil WT	Germ		female	dysgenic	46, XY			MS		33
103	9	1180	394	CGG	TGG	C->T	Ts	Yes		Arg	Trp	NR	Germ		hypospadias		46, XY	no (F) / no (M)	(18 mo)	MS		34
61	9	1180	394	CGG	TGG	C->T	Ts	Yes	85-583	Arg	Trp	no WT	Germ		female		46, XY			nephropathy		28
60	9	1180	394	CGG	TGG	C->T	Ts	Yes	802669	Arg	Trp	unknown	Germ		sex unknown					nephropathy		28
59	9	1180	394	CGG	TGG	C->T	Ts	Yes	802646	Arg	Trp	no WT	Germ		sex unknown					nephropathy		28
58	9	1180	394	CGG	TGG	C->T	Ts	Yes	IV	Arg	Trp	unil WT	Germ		sex unknown					nephropathy		28
57	9	1180	394	CGG	TGG	C->T	Ts	Yes	I	Arg	Trp	unil WT	Germ		sex unknown		46, XY			nephropathy		28
56	9	1180	394	CGG	TGG	C->T	Ts	Yes	TG	Arg	Trp	no WT	Germ		ambiguous		46, XY			nephropathy		28
55	9	1180	394	CGG	TGG	C->T	Ts	Yes	12	Arg	Trp	unil WT	Germ	yes	female					no nephropathy (7 y)		43
53	9	1180	394	CGG	TGG	C->T	Ts	Yes	D5	Arg	Trp	no WT	Germ		ambiguous	testes	46, XY	yes (asymptomatic F)	(18 mo)	nephropathy		29
28	9	1181	394	CGG	CCG	G->C	Tv	No	JK	Arg	Pro	unil WT	Germ		female		46, XY			MS		21
27	9	1180	394	CGG	TGG	C->T	Ts	Yes	LW	Arg	Trp	unil WT	Germ		ambiguous	streak gonads	46, XY	no (M) / ND (F)		MS	rudimentary uterus	21
26	9	1180	394	CGG	TGG	C->T	Ts	Yes	RS	Arg	Trp	unil WT	Germ		ambiguous	dysgenic testes	46, XY			MS		27
25	9	1180	394	CGG	TGG	C->T	Ts	Yes	MW	Arg	Trp	unil WT	Germ		female	streak/dysgenic gonad	46, XX			MS		27
22	9	1180	394	CGG	TGG	C->T	Ts	Yes	SE	Arg	Trp	unil WT	Germ		female	ovaries	46, XX			MS		27
21	9	1180	394	CGG	TGG	C->T	Ts	Yes	PI	Arg	Trp	unil WT	Germ		ambiguous	normal testis/dysgenic testis	46, XY			MS	bicornuated uterus	27
20	9	1180	394	CGG	TGG	C->T	Ts	Yes	AU	Arg	Trp	bil WT	Germ		female		46, XX			MS		27
18	9	1180	394	CGG	TGG	C->T	Ts	Yes	QB	Arg	Trp	unil WT	Germ		ambiguous	dysgenic testes	46, XY	no (F) / no (M)	yes	MS	unilat JGCT/bilat gonadoblastoma	27
17	9	1180	394	CGG	TGG	C->T	Ts	Yes	AM	Arg	Trp	no WT	Germ		ambiguous					MS		27
52	9	1180	394	CGG	TGG	C->T	Ts	Yes	D1	Arg	Trp	bil WT	Germ		female	ovaries	46, XX	no (F) / no (M)		nephropathy		29
14	9	1180	394	CGG	TGG	C->T	Ts	Yes	D3	Arg	Trp	no WT	Germ	yes	ambiguous		46, XY	no (F) / no (M)	(1 y)	MS		30
11	9	1180	394	CGG	TGG	C->T	Ts	Yes	AK / 1658	Arg	Trp	no WT	Germ		female	dysgenic	46, XY			nephropathy		22
8	9	1180	394	CGG	TGG	C->T	Ts	Yes	LB/GOS606	Arg	Trp	unil WT	Germ		female	ovaries	46, XY	no (F) / no (M)		MS		20
6	9	1180	394	CGG	TGG	C->T	Ts	Yes	HD / 7 / GOS368	Arg	Trp	no WT	Germ		female		46, XY	no (M) / ND (F)	(2 y)	MS		20
3	9	1180	394	CGG	TGG	C->T	Ts	Yes	MA/1/GOS372	Arg	Trp	unil WT	Germ		ambiguous		46, XY	no (F) / no (M)		MS		20
62	9	1186	396	GAC	AAC	G->A	Ts	Yes	802629	Asp	Asn	no WT	Germ		ambiguous		46, XY			nephropathy		28
38	9	1186	396	GAC	AAC	G->A	Ts	Yes	2	Asp	Asn	bil WT	Germ	yes	female		46, XX			nephropathy		24
24	9	1186	396	GAC	AAC	G->A	Ts	Yes	WY	Asp	Asn	unil WT	Germ		ambiguous	left Wolffian structure	46, XY			MS	no müllerian structure	27
23	9	1187	396	GAC	GGC	A->G	Ts	No	BE	Asp	Gly	no WT	Germ		female		46, XX	no (F) / no (M)	(14 mo)	MS		27
15	9	1186	396	GAC	AAC	G->A	Ts	Yes	D5	Asp	Asn	unil WT	Germ		female		46, XX	no (F) / no (M)		MS	mutation on paternal allele	30
13	9	1186	396	GAC	AAC	G->A	Ts	Yes	D2	Asp	Asn	unil WT	Germ		ambiguous		46, XY			MS		30
4	9	1186	396	GAC	AAC	G->A	Ts	Yes	SS/12/GOS378	Asp	Asn	unil WT	Germ		male		46, XY	no (F) / no (M)		MS		20
110	9	1193	398	CTG	CCG	T->C	Ts	No	YI	Leu	Pro	unil WT	Germ		female		46, XX			MS		32
37	9	1201	401	CAC	TAC	C->T	Ts	No		His	Tyr	unil WT	Germ		female		46, XX			MS		35

Table 1. Germline WT1 mutations

Base and **Codon**: numbering from the initiation ATG codon.
wt codon and wt AA: wild type codon and wild type amino acid.
Mutant codon: if the mutation is an insertion or a deletion, this is indicated by **del** or **ins** followed by the number of bases inserted or deleted and the position in the codon (**a, b** or **c**). For example, del29a is a deletion of 29 bases including the first base (a) of the codon; ins5c is an insertion of 5 nt at the third position of the codon.
Event: for insertion and deletion mutations, stops are determined by the software.
Type: **Fr** = frameshift; **Ts** = transition; **Tv** = transversion.
CpG: **yes** or **no** indicates whether the mutation involves or not a CpG dinucleotide.
Name: we entered the name of the patients as in the original papers. When the same patient was described several times under different names, we entered the two (three) names separated by /. We left a blank when a patient was described without any name.
Cancer: **uni WT**, unilateral Wilms' tumor; **bil WT**, bilateral Wilms' tumor; **fam WT**, familial Wilms' tumor; **no WT**, no Wilms' tumor; **NR**, Nephrogenic Rest.
Origin: **germ**, germline.
LOH: yes or **no** indicates presence or absence of loss of alleles in the tumor.
mutation in parents: **F**, Father; **M**, Mother.
Nephrectomy: we indicated the age of surgery in years (**y**) or months (**mo**). **R** and **L** refer to Right and Left nephrectomy respectively.
Nephropathy: we entered **MS** for Mesangial Sclerosis only when it was ascertained in the original report.
Other: this column includes miscellaneous information provided for some patients in the original reports: age at diagnosis of WT or follow up without WT; ESRF (End Stage Renal Failure) and age of decease; other malformation; presence of gonadoblastoma; familial history.
Ref: if the same mutation was reported for the same patient in different papers, only one entry corresponding to the first description was made.
In the different columns, we left a blank when the information was not available for a given patient.

Table 2. . Somatic WT1 mutations

File #	Exon	Base	Codon	wt codon	Mutant codon	Event	Type	CpG	Name	wt AA	Mutant AA	Cancer	Origin	LOH	age	clinical features	karyotype/sex	other	Ref
71	1	79	27	CCT	del4b	Stop at 88	Fr.		266672	Pro	Fr.	uni WT	tumor	no	5 y	normal	unknown		36
72	1	229	77	AGC	del34c	Stop at 78	Fr.		802649	Ser	Fr.	uni WT	tumor	del		WAGR	46 XX, del11p13		36
73	1	343	115	CCT	del19c	Stop at 211	Fr.		802501	Pro	Fr.	uni WT	tumor cell line	del		WAGR	46 XY, del11p13		36
78	1	373	125	GCC	del5a	Stop at 128	Fr.		S87-877	Ala	Fr.	uni WT	tumor	yes	11 mo	normal	female		44
80	2	454	152	GTC	del5c	Stop at 177	Fr.		WT12A	Val	Fr.	uni WT	tumor	del	7 mo	developmental delay	46 XY, del11p13		44
75	2	461	154	TTC	TCC	T->C	Ts	No	D.B.	Phe	Ser	uni WT	NR / tumor	no	4 y	normal	female	perilobar NR	45
74	2	481	161	GGT	ins4c	Stop at 179	Fr.		M.W.	Gly	Fr.	uni WT	NR / tumor	yes	11 mo	normal	female	intralobar NR	45
81	2	541	181	CCC	TCC	C->T	Ts	No	BT1	Pro	Ser	uni WT	tumor	no	4 y	minor anomalies	46 XY		44
88	3	580	194	TCG	ins7b	Stop at 224	Fr.		B.M.#7	Ser	Fr.	uni WT	tumor	no	?	normal	unknown		46
97	3	602	201	GGC	GAC	G->A	Ts	No	WT/201	Gly	Asp	uni WT	tumor	del	2 y	WAGR	46 XY, del11p13		47
98	4	714	238	TGG	TGA	G->A	Ts	No	WT 5	Trp	Stop	bi WT	tumor	del	2 y	WAR	female		38
128	6	814	272	GAG	ins4c	ins	Fr.		9177	Glu	Fr.	uni WT	Tumor	no	30 mo		male		39
129	7	901	301	CGA	TGA	C->T	Ts	Yes	9385	Arg	Stop	uni WT	Tumor	yes	12 mo		male		39
90	7	904	302	CGT	del1a	Stop at 306	Fr.		S86-1334	Arg	Fr.	uni WT	tumor	del	7 y	WAGR	46 XY, del11p13		48
130	7	919	307	GCC	del16a	Stop at 375	Fr.		9394	Ala	Fr.	uni WT	Tumor	yes	8 mo		female		39
94	7	934	312	CGG	ins10c	Stop at 316	Fr.		GOS 543	Arg	Fr.	uni WT	tumor	del		WAGR	del11p13		49
87	7	1013	338	TCC	TAC	C->A	Tv	No	K.K.#33	Ser	Tyr	uni WT	tumor			normal	unknown		46
84	8	1084	362	CGA	TGA	C->T	Ts	Yes	B.M.#7	Arg	Stop	uni WT	tumor	no		normal	unknown		46
86	8	1084	362	CGA	TGA	C->T	Ts	Yes	B.T.#53	Arg	Stop	uni WT	tumor	yes		normal	unknown		46
95	8	1084	362	CGA	TGA	C->T	Ts	Yes	GOS 157	Arg	Stop	uni WT	tumor	del		WAGR	del11p13		49
76	8	1096	366	CGT	TGT	C->T	Ts	Yes	WT10	Arg	Cys	uni WT	tumor	no	3 y	normal	unknown		42
131	8	1114	372	AGA	ins2a	ins	Fr.		9561	Arg	Fr.	uni WT	Tumor		34 mo		male		39
77	8	1117	373	CAC	TAC	C->T	Ts	No	S87-52	His	Tyr	uni WT	tumor	yes	13 mo	normal	male		44
79	9	1168	390	CGA	TGA	C->T	Ts	Yes	WT2A	Arg	Stop	uni WT	tumor	?	4 y	WAG	46 XY		44
82	9	1168	390	CGA	TGA	C->T	Ts	Yes	D.J.#11	Arg	Stop	uni WT	tumor	yes		normal	unknown		46
100	9	1168	390	CGA	TGA	C->T	Ts	Yes		Arg	Stop	uni WT	tumor			unknown	unknown		50
91	10	1297	433	CGC	ins1b	ins	Fr.		Wit-24	Arg	Fr.	uni WT	tumor	yes	4 y	normal	male		41
92	10	1297	433	CGC	del2b	del	Fr.		Wit-26	Arg	Fr.	uni WT	tumor	no	2 y	normal	female		41

See legend for Table 1. Specific items are:
LOH: **del** indicates the presence of a constitutional deletion of 11p13.
clinical features: **WAGR**, Wilms' tumor, aniridia, genitourinary abnormalities and mental retardation.

The present version of the database contains 70 germline mutations (Table 1) described either in patients with DDS (19–35), or in patients with genitourinary abnormalities and WT (36–38), or in patients with unilateral or bilateral WT (19,39–43). Somatic mutations described in 28 WT were also registrated (36,38,39,41,42,44–50) (Table 2).

The software package contains routines for the analysis of the WT1 database that were developed with the 4th dimension® (4D) package from ACI. The use of 4D gives access to optimized multicriteria research and sorting tools to select records from any field. Several routines were developed, which can be applied to all or a selection of records: (i) 'Position' studies the distribution of mutations at the nucleotide level to identify preferential mutation sites; (ii) 'Mutational events' is comparable to (i) but also indicates the type of mutational event. For these two options, the corresponding records can be visualized by a single clic on the table; (iii) 'Frequency of mutations' studies the relative distribution of mutations at all sites and sorts them according to their frequency; a graphic representation is also available; (iv) 'Frequency of events' displays a histogram of the different mutational events; (v) 'Distribution of mutations' provides a graphic representation, along the gene, of the mutations that have been sorted from the database according to the different criteria selected by the user; eight charts can be simultaneously drawn; (vi) 'Binary comparison' compares the distribution of mutations between two selected categories of patients, with different possible representations

according either to the amino acid position (1–449), or to the exons (1–10) or to the protein domains (transregulator domain, zinc finger 1–4 and alternative splice regions); (vii) 'Stat exon' studies the distribution of mutations in the different exons, and enables detection of a statistically-significant difference between observed and expected mutations. Data from selected records can be exported to Microsoft Excel®, either as tables or to construct graphics.

In the future, the database will be extended to include mutations described in tumors other than WT. A World Wide Web site is being developed and will be accessible in January 1998 at: http://www.umd.necker.fr

AVAILABILITY

The current version of the database is available on request from C. Je at the following address: jeanpierre@necker.fr. Notification of omissions and errors in the current version would be gratefully received by the corresponding author. The users of the database are requested to cite the current article.

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