

## Indication criteria for genetic testing Evaluation of validity and clinical utility

german society of human  
genetics  
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### Indication criteria for disease: *Angelman-Syndrome [UBE3A]*

#### 1. General information on authorship

##### Name and address of institution:

Name: *Institute of Human Genetics, Medical University Lübeck*  
Address: *Ratzeburger Allee 160*  
Postcode: *D-23538*  
City: *Lübeck*  
Tel.: *+49-451-500-2620*  
Fax: *+49-451-500-4187*  
E-mail: *marianne.schirr@uk-sh.de*  
Internet: *www.humangenetik.mu-luebeck.de*

##### Head of the institution:

Name: *Prof. Dr. Gabriele Gillesen-Kaesbach*  
Tel.: *+49-451-500-2620*  
Fax: *+49-451-500-4187*  
E-mail: *g.gillesen@uk-sh.de*

##### Author of this text, date:

Name: *Prof. Dr. Eberhard Schwinger*  
Tel.: *+49-451-500-6055*  
Fax: *+49-451-500-4187*  
E-mail: *schwinger@uni-luebeck.de*  
Date: *05.06.2007*

##### Reviewer, validation date:

Name: *Prof. Dr. Bernhard Horsthemke*  
Tel.: *+49-201-723-4556*  
Fax: *+49-201-723-5900*  
E-mail: *bernhard.horsthemke@uni-due.de*  
Date: *16.07.2007*

##### Translator, translation date:

Name: *Prof. Dr. Ulrich Langenbeck*  
E-mail: *Ulrich.Langenbeck@gmx.net*  
Date: *09.03.2008*

##### Re-editor, date:

Name:  
Tel.:  
Fax:  
E-mail:  
Date:

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##### Address of chairman

Institut für Humangenetik  
Universität Erlangen-Nürnberg  
Schwabachanlage 10  
91054 Erlangen  
Tel 0049 (0)9131-852 2318  
Fax 0049 (0)9131-209297  
reis@humgenet.uni-erlangen.de

##### GfH-Office

Dipl.-Soz. Christine Scholz  
Inselkammerstr. 4  
82008 München-Unterhaching  
Telefon+49 (089) 614 56 95 9  
Telefax +49 (089) 55 02 78 56  
organisation@gfhev.de

##### Bank Details

Postbank München  
Konto 231 394 805  
BLZ 700 100 80

##### IBAN

DE19 7001 0080 0231 3948 05

##### BIC

PBNK DEFF

##### Vereinsregister München

VR 12341

## 2. Disease characteristics

2.1 Name of the Disease (Synonyms): *Angelman syndrome*

2.2 OMIM# of the Disease: *105830*

2.3 Name of the Analysed Genes or DNA/Chromosome Segments:  
*UBE3A / #15q11-q13*

2.4 OMIM# of the Gene(s): *601623*

2.5 Mutational Spectrum:  
*70% maternal deletion 15q11-q13*  
*1% paternal uniparental disomy [upd(15)pat]*  
*3% imprinting defect*  
*15% mutations in UBE3A gene*  
*10% other*

2.6 Analytical Methods:  
*methylation test, FISH, microsatellite analysis, MLPA;*  
*if methylation is normal -> search for UBE3A mutations*

2.7 Analytical Validation  
*parallel analysis of positive and negative controls*

2.8 Estimated Frequency of the Disease in Germany  
(Incidence at birth ("birth prevalence") or population prevalence):  
*prevalence at birth 1:12,000-1:20,000*

2.9 If applicable, prevalence in the ethnic group of investigated person:  
*not applicable*

2.10 Diagnostic Setting:

	yes	no
A. (Differential)diagnostics	<input checked="" type="checkbox"/>	<input type="checkbox"/>
B. Predictive Testing	<input type="checkbox"/>	<input checked="" type="checkbox"/>
C. Risk assessment in Relatives	<input checked="" type="checkbox"/>	<input type="checkbox"/>
D. Prenatal	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Comment: *none*

### 3. Test characteristics

		Genotyp bzw. Krankheit	
		vorhanden	fehlend
Test	pos.	A	B
	neg.	C	D

A: richtig Positive      C: falsch Negative  
 B: falsch Positive      D: richtig Negative

Sensitivität:               $A/(A+C)$   
Spezifität:                 $D/(D+B)$   
pos. prädikt. Wert:       $A/(A+B)$   
neg. prädikt. Wert:       $D/(C+D)$

#### 3.1 Analytical Sensitivity

(proportion of positive tests if the genotype is present)

*practically 100%*

#### 3.2 Analytical Specificity

(proportion of negative tests if the genotype is not present)

*practically 100%*

#### 3.3 Clinical Sensitivity

(proportion of positive tests if the disease is present)

The clinical sensitivity can be dependent on variable factors such as age or family history. In such cases a general statement should be given, even if a quantification can only be made case by case.

*85-90%*

#### 3.4 Clinical Specificity

(proportion of negative tests if the disease is not present)

The clinical specificity can be dependent on variable factors such as age or family history. In such cases a general statement should be given, even if a quantification can only be made case by case.

*practically 100%*

#### 3.5 Positive clinical predictive value

(life time risk to develop the disease if the test is positive).

*practically 100%*

#### 3.6 Negative clinical predictive value

(Probability not to develop the disease if the test is negative).

Assume an increased risk based on family history for a non-affected person. Allelic and locus heterogeneity may need to be considered.

Index case in that family had been tested:

*practically 100%*

Index case in that family had not been tested:

*can only be clarified through analysis of the non-affected individual*

## 4. Clinical Utility

### 4.1 (Differential)diagnosis: The tested person ist clinically affected

(To be answered if in 2.10 "A" was marked)

4.1.1 Can a diagnosis be made other than through a genetic test?

no  (continue with 4.1.4)

yes

clinically

imaging

endoscopy

biochemistry

electrophysiology

other (please describe)

4.1.2 Describe the burden of alternative diagnostic methods to the patient

4.1.3 How ist the cost effectiveness of alternative diagnostic methods to be judged?

4.1.4 Will disease management be influenced by the result of a genetic test?

no

yes

Therapy (please describe)

Prognosis (please describe)

Management (please describe)

#### **4.2 Predictive Setting: The tested person is clinically unaffected but carries an increased risk based on family history**

(To be answered if in 2.10 "B" was marked)

4.2.1 Will the result of a genetic test influence lifestyle and prevention?

If the test result is positive (please describe)

If the test result is negative (please describe)

4.2.2 Which options in view of lifestyle and prevention does a person at-risk have if no genetic test has been done (please describe)?

#### **4.3 Genetic risk assessment in family members of a diseased person**

(To be answered if in 2.10 "C" was marked)

4.3.1 Does the result of a genetic test resolve the genetic situation in that family?

*No.*

4.3.2 Can a genetic test in the index patient save genetic or other tests in family members?

*see 4.3.1*

4.3.3 Does a positive genetic test result in the index patient enable a predictive test in a family member?

*not applicable*

#### **4.4 Prenatal diagnosis**

(To be answered if in 2.10 "D" was marked)

4.4.1 Does a positive genetic test result in the index patient enable a prenatal diagnostic?

*Yes.*

#### **5. If applicable, further consequences of testing**

Please assume that the result of a genetic test has no immediate medical consequences. Is there any evidence that a genetic test is nevertheless useful for the patient or his/her relatives? (Please describe)

*Parents will finally know the cause of the disease.*