HUMAN GENETICS EXPERT OPINION

Court Expert Opinion on Order for Evidence | Prenatal Liability / Wrongful Birth

KBG syndrome due to a de novo ANKRD11 mutation | Parents without abnormalities | Severe intellectual disability | Was prenatal diagnosis warranted? | Liability of the attending gynecologist and the prenatal diagnostic center

Case Number	LG [City] - Ref. [XX] O [XXXX]/[YY] (Sample Case)
Client	Regional Court [City], [Civil Division], Order for Evidence dated [Date]
Plaintiffs	Anna and Michäl K. [fictitious], as legal representatives of their son Felix K. and on their own behalf
Defendants	1. Dr. med. Sabine H. [fictitious], specialist in gynecology; 2. Prenatal Center [Name] GmbH [fictitious]
Expert	Prof. Christian T. Thiel, M.D., MBA
Qualifications	Specialist in Human Genetics; University Hospital Erlangen; 30 years of clinical and scientific experience; expert witness for courts and insurance carriers
Date	March 28, 2026
Affected child	Felix K. [fictitious], born [date], male; Diagnosis: KBG syndrome (OMIM #148050); ANKRD11 c.6388C>T (p.Arg2130*), de novo, ACMG Class 5; severe intellectual disability, epilepsy, craniofacial dysmorphia
Key question	Would the sonographic findings from prenatal detailed diagnostics, assuming findings were recorded and interpreted in accordance with guidelines, have provided grounds for recommending invasive chromosomal or exome testing that would have detected the de novo mutation and thus the child's KBG syndrome prenatally?

Statement pursuant to Sections 407, 407a of the German Code of Civil Procedure (ZPO)

The undersigned was appointed by the Regional Court of [City] as a neutral expert and declares that he has prepared this expert opinion impartially, to the best of his knowledge and belief, and without regard to any interests of the parties. He affirms that he has no personal or financial relationship with the parties. With regard to the question of classification under legal categories (wrongful birth, duty to inform, causation), this expert opinion is limited to the medical-scientific basis, while the legal assessment is the responsibility of the court.

Preliminary Remarks: Legal Framework of the Wrongful Birth Claim

This expert opinion addresses the context of so-called wrongful birth liability. The Federal Court of Justice (BGH) has consistently recognized in its case law (e.g., BGH VI ZR 386/99; BGH VI ZR 198/01) that parents of a child with severe disability

may be able to assert claims for damages against the treating physicians if a medical error (insufficient information, incomplete diagnosis, incorrect interpretation of findings) prevented the mother from making an independent decision regarding the continuation of the pregnancy.

The decisive factor is not whether the child "should have been prevented," but whether **the parents were deprived of the opportunity to make an informed decision due to medical negligence.** The expert opinion must therefore clarify: (1) Were there any sonographic abnormalities that would have warranted further diagnostic testing? (2) Would this diagnostic testing have revealed the de novo mutation? (3) Was the collection and communication of findings by the defendants in accordance with guidelines?

1. Court's Mandate and Questions

By order for the taking of evidence dated [Date], the Regional Court of [City] commissioned the undersigned to provide an expert opinion on the following questions:

1. What sonographic findings were present during the plaintiff's pregnancy, and did their assessment and documentation comply with the state of the art at the time of the examination and the guidelines of the DGGG and the DEGUM?
2. Would the sonographic abnormalities present or detectable during an examination in accordance with the guidelines have given rise, according to the state of the art at the time, to a recommendation for invasive prenatal diagnostics (amniocentesis with chromosomal analysis and/or prenatal exome sequencing)?
3. Could the de novo ANKRD11 c.6388C>T (p.Arg2130*) mutation detected postnatally in the child have been diagnosed with sufficient probability through prenatal exome sequencing?
4. Had the plaintiff been properly informed about the findings and their implications, would she have, with a sufficient degree of probability, requested further diagnostic testing, and would an abnormal finding have provided the opportunity to make an independent decision regarding the continuation of the pregnancy?
5. Is there a medical error in treatment or counseling on the part of one or both defendants?

2. Investigation Materials and Methodology

2.1 Submitted documents

- Complete prenatal record documentation of the pregnancy
- Ultrasound reports First-trimester screening (11+0 to 13+6 weeks of gestation): Report by Defendant 1 (Dr. H.)
- Detailed diagnostic reports for the 20th week of gestation (organ screening) and the 30th week of gestation: Defendant 2 (Prenatal Center)
- Ultrasound images and saved loops (if available and submitted)
- Postnatal clinical-genetic report (University Hospital [X], Date: [Date])
- Molecular genetic report: Trio exome sequencing (child + both parents); ANKRD11 c.6388C>T de novo mutation confirmed; both parents wild-type
- Pediatric Progress Notes: Felix K. (Age 0–5 years)
- Statement of claim, answer to the complaint by both defendants, arguments of the parties
- Relevant guidelines: DEGUM staged diagnostics, DGGG guidelines for prenatal diagnostics, ACMG recommendations for prenatal exome sequencing, ISUOG guidelines

2.2 Methodology of the expert evaluation

The assessment is conducted in two steps: First, the ex-ante standard is applied—was the assessment of findings at the time of the examinations in accordance with the guidelines? Second, a hypothetical assessment is made of what would have been diagnosed had the procedure been in accordance with the guidelines and whether this would have interrupted the causal chain leading to the harm. The benchmark for comparison is a diligent specialist in the relevant field (gynecology; prenatal diagnostics, DEGUM Level III) at the time of treatment.

3. Facts

3.1 Course of pregnancy and prenatal findings

The plaintiff, Anna K., born [date], [age] years old, was in her first pregnancy. Both parents are clinically unremarkable and have no known pre-existing conditions. There was no known family history of genetic disorders. The mother's age was under 35, so there was no increased age-related chromosomal risk.

According to the defendant's documentation, the prenatal examinations proceeded as follows:

Date / Examination	Documented Findings	Expert Assessment
11+3 weeks of gestation: ETS (Dr. H.)	NT 1.8 mm (normal); nasal bone visualized; PAPP-A and free beta-hCG unremarkable; risk of trisomy 21 1:4200	No evidence of chromosomal abnormality; ETS performed according to guidelines
20+1 weeks of gestation: Organ screening (Prenatal Center)	Biometry: BPD, FL, AC normal; heart activity normal; organs documented as normal; 'unremarkable findings'	POINT OF CONTROVERSY: Microcephaly cutoff value? Cerebellum? Corpus callosum?
20+1 weeks gestation: Documented head circumference	BPD 47 mm (10th percentile); HC 181 mm (10th percentile)	Head circumference at the lower limit of normal; follow-up not documented, recommended
30+2 weeks gestation: Follow-up ultrasound (Prenatal Center)	Biometry: BPD 75 mm (5th percentile); FOC 278 mm (3rd percentile); FL normal; 'mild growth restriction, follow-up recommended'	**CU < 3 cm = formal microcephaly; recommendation for "follow-up" without explanation of causes or indication for further evaluation is INCORRECT**
Further diagnostic testing recommended?	**NO – neither by Defendant 1 nor Defendant 2**	**According to guidelines for microcephaly < 3 cm: Recommendation for human genetic counseling and, if necessary, prenatal exome sequencing MANDATORY**

3.2 Postnatal diagnosis

Felix K. was born in the [gestational week]. The following abnormalities were noted postnatally: marked microcephaly (head circumference < 3rd percentile), characteristic craniofacial dysmorphic features (macrodontia, broad nose, short philtrum, low-set ears), delayed developmental milestones, feeding difficulties in the neonatal period. At 8 months of age, first manifestation of symptomatic epilepsy.

Molecular genetic trio exome sequencing at 18 months of age revealed a de novo mutation in the ANKRD11 gene. Both parents are wild-type carriers. The diagnosis of KBG syndrome was confirmed.

Postnatal molecular genetic findings
Child: ANKRD11 c.6388C>T (p.Arg2130*) - heterozygous - DE NOVO
Father: ANKRD11 wild-type (mutation not detected)
Mother: ANKRD11 wild-type (mutation not detected)
Classification: Pathogenic (ACMG Class 5) | de novo origin confirmed **Diagnosis: KBG syndrome (OMIM #148050)**

4. Family history and genetic background

Both parents are clinically and molecularly normal (trio exome sequencing: both wild-type for the ANKRD11 mutation). There is no known history of genetic disorders, intellectual disabilities, or malformation syndromes on either side of the family.

This is the defining characteristic of a de novo mutation: it arises for the first time in the germ cell of one of the parents or during early embryogenesis and is neither familial nor predictable based on family history. **This circumstance is decisive for the question of the duty of care:** Since there was no family history, the defendants had no clinical indication of an increased genetic risk. The indication for further diagnostic testing would therefore have had to arise exclusively from the ultrasound findings—and these were present in accordance with guidelines.

The risk of recurrence in the parents' future pregnancies is low (< 1% for gonadal mosaics in the mutation-carrying parent), but not zero. This is relevant for the family's genetic counseling.

5. KBG Syndrome: Genetic Basis, Clinical Presentation, and Phenotype

5.1 Genetic Basis

KBG syndrome (OMIM #148050) is a rare autosomal dominant disorder caused by pathogenic variants—primarily loss-of-function variants (nonsense, frameshift, large deletions)—in the ANKRD11 gene (Ankyrin Repeat Domain 11; 16q24.3). [1,2] In the majority of cases (approximately 70–85%), the disorder arises as a de novo mutation with no family history. [1,3]

ANKRD11 encodes a chromatin regulatory protein involved in controlling gene expression during brain development. Loss of function leads to disturbances in cortical neurogenesis, which explains intellectual disability as the primary symptom. [2,4]

5.2 Clinical Spectrum of KBG Syndrome

KBG syndrome is characterized by the following key symptoms, which are present in the majority of affected individuals:

Clinical feature	Prevalence in KBG	Detected in Felix K.?
Intellectual disability (mild to severe)	> 95%	Yes - severe (IQ < 40)
Microcephaly	60–70%	Yes - detectable prenatally from the 30th week of gestation
Characteristic facial features (macrodontia, short philtrum)	80–90%	Yes - described postnatally
Short stature	70%	Yes
Epilepsy	30–50%	Yes - starting at 8 months
Behavioral disorders (ASD spectrum)	40–60%	Yes - suspected
Skeletal abnormalities (brachydactyly, rib abnormalities)	40–60%	Mild brachydactyly

5.3 Prenatal detectability of KBG syndrome

This is the central point of the expert opinion. KBG syndrome does not have a specific prenatal ultrasound pattern that allows for a direct sonographic diagnosis. **However, microcephaly is the most common and clinically most severe symptom and can—if detected in accordance with guidelines—serve as an indicator for further diagnostic testing.**

Microcephaly is defined prenatally as a head circumference (HC) below the 3rd percentile for gestational age. At 30 weeks of gestation, this corresponds to an HC < 281 mm (Hadlock reference values). The HC of 278 mm documented for Felix K. at 30 weeks of gestation was below this threshold and thus met the definition of prenatally detectable microcephaly.

6. Relevant guidelines and the duty of medical care

6.1 Current guidelines on prenatally detectable microcephaly

At the time of the pregnancy ([Year]), the following guidelines and recommendations, which are relevant for assessing the standard of medical care, were in effect:

- DEGUM Guideline on Prenatal Diagnostics (Level II/III): If the risk is < 3%, an additional examination including fetal MRI skull diagnostics and referral to a Level III prenatal medical center is indicated
- DGGG Guideline on Prenatal Diagnostics: Microcephaly is considered a 'soft marker' / structural abnormality that warrants genetic counseling and, if necessary, invasive diagnostics
- ACMG/SMFM Guidelines on Prenatal Exome Sequencing (2020): In cases of prenatally detectable structural anomalies without an explanatory chromosomal finding,

prenatal exome sequencing is indicated as a diagnostic tool and should be offered [5,6]

– ISUOG Guidelines on Fetal Neurology (2020): A head circumference (HC) < 3rd percentile should be classified as isolated prenatal microcephaly and warrants cranial MRI as well as genetic evaluation [7]

6.2 Mandatory content of the communication of findings in cases of microcephaly

Regardless of the diagnostic procedure itself, the physician has an independent duty to inform: The pregnant woman must be informed of any prenatally detectable abnormal findings, educated about possible causes, and advised on the possibility of further diagnostic testing (invasive or non-invasive). This duty arises from the Genetic Diagnosis Act (Section 15 GenDG: Duty to Inform Before and After Genetic Diagnosis) as well as from general medical duties to inform.

Defendant 2 (Prenatal Center) merely documented “mild growth retardation, follow-up recommended” in its findings report at the 30th week of gestation. **No documentation exists, nor did it occur verbally according to the plaintiff’s account, of an explanation to the plaintiff regarding the significance of a head circumference < 3 standard deviations (prenatal fulfillment of the definition of microcephaly), possible genetic causes, and the possibility of prenatal exome sequencing.**

7. Expert Analysis of Errors

7.1 Evaluation of Findings by Defendant 1 (Dr. H.) – First-Trimester Screening

The first-trimester screening at 11+3 weeks of gestation performed by Defendant 1 was conducted in accordance with guidelines, based on the available documentation. Nuchal translucency, nasal bone, biochemical screening, and risk calculation correspond to the standard according to the documented findings. At the time of the first-trimester screening, microcephaly is not detectable (biometric reference values at this gestational week are not indicative of later microcephaly).

Defendant 1: **No error in the first-trimester screening is apparent.** Responsibility lies with the Prenatal Center (Defendant 2) starting with the organ screening (20th week of gestation).

7.2 Evaluation of findings by Defendant 2 (Prenatal Center) – Organ screening at 20 weeks of gestation

At 20+1 weeks of gestation, a crown-rump length (CRL) of 181 mm (10th percentile) was recorded. Although this value is still within the normal range, it is at the lower limit. According to current guidelines, this finding alone would have warranted:

1. A documented recommendation for follow-up monitoring of head biometry (not performed)
2. Required a mention during the consultation as 'lower normal range, follow-up monitoring recommended' (not documented)

This aspect of the findings alone does not yet constitute a serious error, but it does constitute an initial documentation requirement.

7.3 Findings Assessment Defendant 2 - Follow-up Ultrasound at 30 Weeks Gestational Age - CRITICAL ERROR

Core error: Follow-up ultrasound at 30+2 weeks of gestation

A HC of 278 mm at 30+2 weeks of gestation corresponds to the < 3rd percentile according to Hadlock standard curves (threshold value approx. 281 mm). This formally meets the prenatal definition of microcephaly. Defendant 2 communicated this finding as 'mild growth retardation' without:

1. Informing the plaintiff about the finding of prenatally detectable microcephaly (head circumference < 3rd percentile)
2. Providing information about possible causes (genetic cause, CNS malformation, infection)
3. Recommending a fetal MRI of the skull
4. Offer genetic counseling and prenatal exome sequencing as a diagnostic option
5. Offer a referral to a DEGUM Level III center / prenatal medical expert center

These omissions constitute a breach of the prenatal duty of care and the physician's duty to inform. They are not covered by the physician's discretion: Once a contraindication (KU) <
3. patient, the described measures are not optional but mandatory actions according to current guidelines.

7.4 Would prenatal exome sequencing have detected the de novo mutation?

This question is decisive for causality. The undersigned assesses it as follows:

Diagnostic detectability of the de novo mutation via prenatal exome sequencing

Prenatal exome sequencing (prenatal trio WES: child + both parents) had established itself as an available diagnostic tool at the time of the pregnancy ([Year]). The 2020 ACMG/SMFM recommendations list prenatal structural anomalies without an explanatory conventional chromosomal finding as an indication. [5,6]

According to current studies, the detection rate of de novo mutations by prenatal trio WES in fetuses with microcephaly is approximately 30–50% [8,9]. ANKRD11 loss-of-function variants such as p.Arg2130* are detected with a high degree of certainty by standard exome sequencing (coverage of the ANKRD11 locus > 98% in common exome panels).

It is highly probable that a prenatally indicated trio WES would have detected the de novo ANKRD11 c.6388C>T mutation.

Limitation: Prenatal whole-exome sequencing is not a routine procedure and will not always provide a definitive result. However, the point here is that, had the procedure been conducted in accordance with guidelines (diagnosis of microcephaly → counseling → offer of prenatal whole-exome sequencing), the plaintiff would have had the option to undergo this diagnostic test. The denial of this choice is the event giving rise to liability—regardless of how the plaintiff would ultimately have decided.

8. Assessment of Causation

8.1 Causality giving rise to liability: error and harm

The following chains of causation are relevant for wrongful birth liability:

1. **Causal chain 1 – Diagnostic error:**

Head circumference 278 mm (< 3rd percentile) at 30 weeks' gestation -> prenatal microcephaly -> duty to inform and offer further diagnostic testing -> failed to do so -> plaintiff was not informed -> decision-making option thwarted.

2. **Causal chain 2 – Failure to inform:**

Even if one considers the KU value to be borderline (which is incorrect according to the guidelines): Communicating the diagnosis as "mild growth retardation, follow-up recommended" without informing the patient about genetic differential diagnoses and without offering prenatal exome sequencing violates the duty to inform.

3. **Causal chain 3 – Extent of harm:**

Had the plaintiff been informed of the prenatally detectable microcephaly and the possibility of further diagnostic testing, and had the prenatal WES detected the de novo mutation, she would have had the opportunity to make an autonomous decision regarding the continuation of the pregnancy. This opportunity was denied to her.

8.2 Plaintiff's Hypothetical Intent to Decide

The court will have to examine whether the plaintiff would have requested further diagnostic testing had she received proper information, and how she would have decided in the event of an abnormal finding (so-called hypothetical decision-making intent). From a human genetic perspective, the following must be noted:

- KBG syndrome, characterized by severe intellectual disability and epilepsy, is among the conditions for which, according to available studies, a high percentage of parents would consider terminating the pregnancy
- The ANKRD11 mutation is clearly pathogenic and associated with a severe phenotype—a "mild" variant of KBG syndrome is not to be expected with this nonsense mutation
- The plaintiff's decision upon learning of the findings is a highly personal decision that must not be prejudged by the expert and is the responsibility of the court

8.3 Distinction: Fate versus Error

The defendants are likely to argue that de novo mutations are unpredictable and that the parents did not face an increased risk of recurrence. This objection fails to recognize the basis of the claim: **the issue is not the predictability of the mutation, but rather the sonographically detectable indicative finding (microcephaly), which, if interpreted and communicated in accordance with guidelines, would have enabled the plaintiff to make an informed decision.**

De novo mutations are biologically unavoidable. The error lies not in the occurrence of the mutation, but in the failure to diagnose a detectable finding and the failure to provide information about it.

9. Conclusion / Expert Assessment

Summary of the expert findings

1. Confirmed diagnosis: Felix K. suffers from KBG syndrome (OMIM #148050), caused by the de novo mutation ANKRD11 c.6388C>T (p.Arg2130*, ACMG Class 5). The de novo origin is confirmed by trio exome sequencing of both clinically unremarkable parents. There was no familial risk factor in the medical history.
2. Prenatally detectable indicative finding: At 30+2 weeks of gestation, the head circumference was 278 mm, which, according to Hadlock standards, falls below the 3rd percentile and meets the prenatal definition of microcephaly. According to current guidelines (DEGUM, DGGG, ISUOG), this finding would have required structured evaluation, counseling, and the offer of further diagnostic testing.
3. Failure by Defendant 2: Defendant 2 communicated the finding as “mild growth retardation” without informing the plaintiff of the significance of the finding and without offering prenatal exome sequencing as a diagnostic option. This constitutes a breach of the medical duty to communicate findings and the duty to inform.
4. No breach of duty by Defendant 1: The first-trimester screening performed by Defendant 1 complied with the standard guidelines. Microcephaly was not detectable in the first trimester. No breach of duty by Defendant 1 can be established.
5. Diagnostic feasibility: Prenatal trio exome sequencing would, with a high degree of probability, have detected the de novo ANKRD11 mutation if indicated (microcephaly < 3 cm). The detection rate of de novo mutations in cases of prenatally detectable microcephaly via prenatal trio WES is approximately 30–50%.
6. Causal connection: Defendant 2’s failure to communicate the findings and provide information deprived the plaintiff of the opportunity to make an informed decision regarding the continuation of the pregnancy. This constitutes the event giving rise to damages within the meaning of the Federal Court of Justice’s (BGH) wrongful birth case law.

The above expert findings are rendered to the best of my knowledge and belief, impartially and conscientiously, in accordance with Sections 407 and 407a of the German Code of Civil Procedure (ZPO). The undersigned certifies that he is not in a relationship of dependency with any of the parties.

9a. Limitations of the Human Genetic Expert Opinion and Recommendations for the Court

This human genetic expert opinion addresses the medical and scientific questions. To ensure a complete clarification of the facts, the undersigned recommends that the court obtain the following supplementary expert opinions:

1. Prenatal medical / DEGUM Level III report: Was the organ sonography performed during the Was the care provided at 20 weeks of gestation in accordance with guidelines? Were the fetal head measurements recorded and documented correctly? Is the prenatal center's assessment at 30 weeks of gestation technically accurate?
2. Child psychiatric/neuropediatric expert opinion: What specific sequelae has Felix K. suffered as a result of KBG syndrome? What is the lifetime additional need for care and support (amount of damages)?
3. If necessary, taking of evidence regarding the plaintiff's hypothetical decision: Would the plaintiff have opted for prenatal WES diagnostics if she had been properly informed? How would she have decided in the event of an abnormal finding?

9b. Care-related recommendations for Felix K.

Regardless of the outcome of the legal dispute, the following measures are indicated for Felix K. from a human genetic perspective:

- Regular neuropediatric follow-up, including EEG (risk of epilepsy 30–50%, already manifest)
- Intensive early intervention (speech therapy, occupational therapy, special education)
- Co-management by child and adolescent psychiatry in cases of suspected autism spectrum disorder
- Dental care: Macrodontia as a key symptom of KBG requires specialized dental treatment
- Human genetic family counseling: Low risk of recurrence for siblings (< 1% for gonadal mosaicism), but not zero; offer prenatal diagnosis for future pregnancies
- Application for GdB: GdB 80–100 due to severe intellectual disability, epilepsy, and developmental delay; H (helplessness) and G designations likely

10. References

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Erlangen, March 28, 2026

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