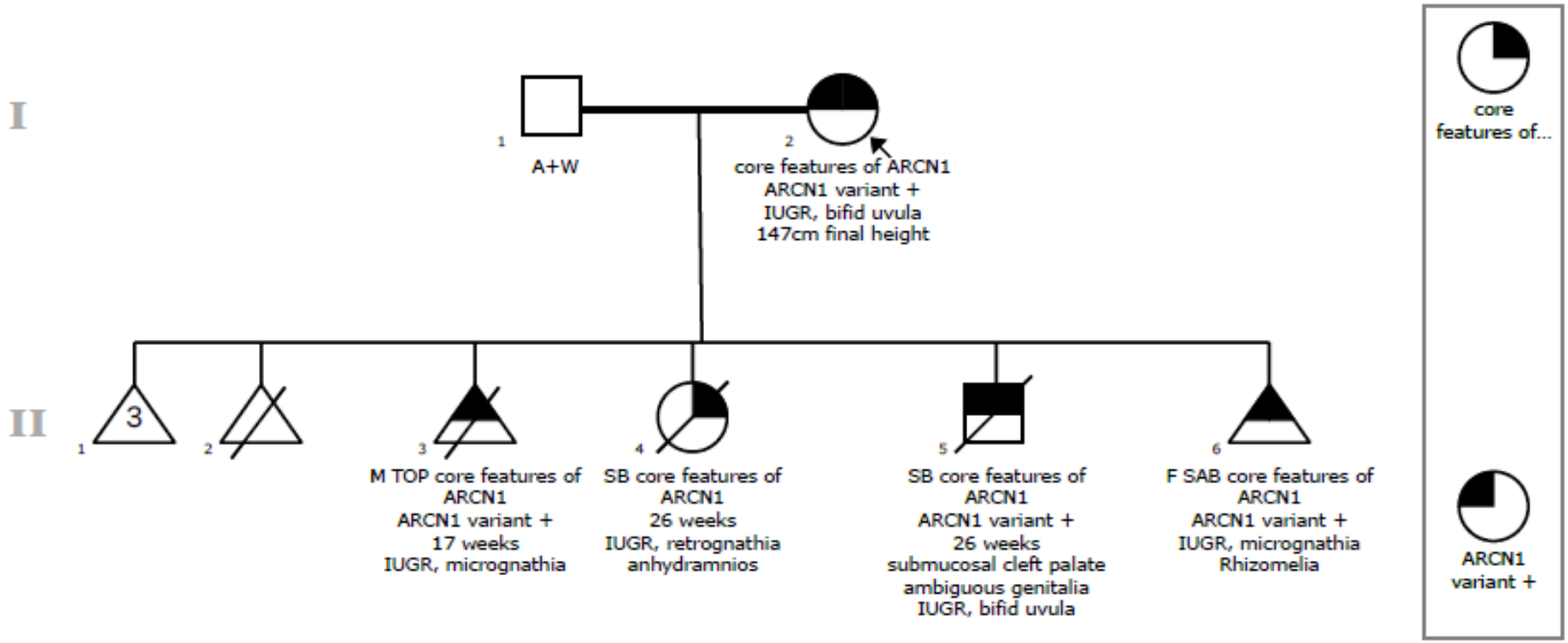
Supplemental Data. Additional Case Information.

Subject N1 was referred to Department of medical genetics, Oslo University Hospital at age 1 year and 6 months. Her main concern was a newly diagnosed hepatoblastoma, but she also presented with short stature, feeding difficulties and micrognathia. Subject X is the first child of healthy, un-consanguineous parents. She was delivered with cesarean section at 30 weeks of gestation because of intrauterine growth restriction and preeclampsia. She was small for gestational age with birth weight 1140 g, length 36 cm and head circumference 27.2 cm. She needed support with ventilation the first 2 months of life and persistent nutritional support. At age 2 years and 6 months, her eating skills are significantly delayed and she receives part of her nutrition through a percutaneous endoscopic gastrostomy. Developmentally, she is considered mildly delayed. On physical examination, she presents with some minor anomalies including micrognathia, bilateral preauricular pit, clinodactyly of fifth finger and fetal pads. Her extremities appear proportionately.

The patient was acute hospitalized at age 15 months with circulatory collapse and hemoperitoneum due to rupture of a tumor in the liver. The tumor was localized in liver segment 5 with histopathology compatible with a hepatoblastoma with embryonal differentiation, intermediate risk. The liver segment 5, the gallbladder with a lymph node and two lymph nodes localized in the hilus were laparoscopic resected and she is treated with pre- and postoperative chemotherapy. So far, she has responded well to treatment without signs of relapse. She is regularly followed at Department of Pediatric Oncology.

Exome sequencing of the patient and her parents with analysis of a gene panel for developmental disorders revealed a de novo heterozygous *ARCN1* loss of function variant: c.934C>T (p.Arg312*)(NM_001655.4). Further investigations have revealed normal echocardiography, normal MR Caput, normal ophthalmologic examination and normal array CGH analysis. Unfortunately, no molecular testing was performed in the hepatoblastoma sample.

Supplemental Figure 1. Pedigree of Family with *ARCN1*-related Syndrome including proband (F1) and affected fetuses. Legend: A+W (alive and well), F (female), IUGR (intrauterine growth restriction), M (male), SAB (spontaneous abortion), SB (stillbirth), TOP (termination of pregnancy).



Supplemental Table 1a: N-glycan abnormalities in ARCN1-related syndrome.

ARCN-1 N-glycan Changes

Transient increase of Man5 and Mono-Gal

N-Glycan	P1	P2	P3	P4	P5 (previously reported by Reunert et al)	Reference Low	High
	well visit	well	sick	1 w before sick	sick		
	0.07	0.12	0.11	0.05	0.05	0.01	0.07
	0.16	0.23	0.19	0.08	0.10	0.01	0.10
	0.37	0.48	0.51	0.2	0.30	0.00	0.24
	0.52	1.00	1.21	0.41	0.77	0.02	0.42
	1.41	2.25	3.51	1.32	2.99	0.22	1.20
	3.45	**4.63**	**8.71**	**3.58**	**9.23**	0.81	3.13
	0.13	0.22	1.00	0.25	0.38	0.00	0.42
	2.88	**1.62**	**4.78**	**2.01**	**2.88**	0.67	1.88
	0.90	1.14	1.02	0.96	1.35	0.40	1.33
	40.13	27.60	23.03	41.14	32.92	25.55	55.21

Supplemental Table 1b: Normalization of N-glycans in patient previously reported by Reunert et al.

N-glycans Normalize in ARCN1-related syndrome (P5, a previously reported European patient)

N-Glycan	P5	P5	P5	P5	P5
	Viral sickness	2W post	1M post	4M post	5M post
	0.05	0.03	0.03	0.02	0.03
	0.10	0.04	0.05	0.03	0.03
	0.30	0.11	0.15	0.13	0.12
	0.77	0.30	0.19	0.16	0.13
	2.99	1.17	0.69	0.56	0.46
	9.23	3.49	2.00	1.58	1.37
	0.38	0.18	0.16	0.12	0.08
	2.88	1.60	1.21	1.14	0.85
	1.35	1.05	1.08	0.85	0.60
	32.92	47.97	47.67	53.90	48.77