Astrocyte elevated gene-1 overexpression in histologically favorable Wilms tumor is related to poor prognosis

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Abstract *Objective:* Astrocyte elevated gene-1 (AEG-1) is associated with tumorigenesis and progression in various types of human cancers. However, the status of AEG-1 expression and its significance in Wilms tumor are still unclear. In this study, we investigated the expression of AEG-1 and evaluated its clinical and prognostic significance in favorable-histology Wilms tumor (FHWT).

Materials and methods: Immunohistochemistry was performed to examine AEG-1 protein expression in paraffin-embedded tissues from 38 FHWT patients. All patients underwent radical nephrectomy from January 2003 to June 2008 with subsequent therapy according to National Wilms Tumor Study Group protocols. Statistical analyses were performed to evaluate the association between AEG-1 expression and clinical parameters.

Results: We found high AEG-1 expression in 17 of 38 (44.7%) patients. AEG-1 expression was significantly correlated with clinical stage ($p = 0.019$) and status of recurrence ($p = 0.023$). Importantly, patients with high AEG-1 expression had a shorter disease-free survival and overall survival compared with those with low AEG-1 expression ($p = 0.011$ and $p = 0.013$).

Conclusion: AEG-1 expression is associated with FHWT outcome in this study, and AEG-1 may represent a novel and valuable predictor for prognostic evaluation of FHWT patients.

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Introduction

Wilms tumor (WT), also known as nephroblastoma, is the most common cancer of the urinary tract affecting 7/1 000 000 children under the age of 15 years [1]. During the last few decades, refinements in multimodal therapy, including surgery, adjuvant chemotherapy, and selective radiation therapy, have dramatically improved the prognosis of children with WT. Overall, tumor-free survival is now greater than 90% for patients with stage I, II, or III favorable-histology Wilms tumor (FHWT). However, there are cases of FHWT that either fail to respond and/or relapse during or following completion of standardized

National Wilms Tumor Study Group (NWTSG) treatment protocols [2]. Although previous studies have shown some aberrant molecular events, such as loss of heterozygosity (LOH) for chromosome 16q or 1p [3,4], chromosome 1q gain [5—9], p53 mutation [10], VEGF upregulation [10], B7-H1 expression [11] and bcl-2 negative expression [12] responsible for FHWT progression and recurrence, other biological factors associated with poor prognosis remain largely unknown.

Astrocyte elevated gene-1 (AEG-1), also known as Metadherin (MTDH) and LYRIC, was originally identified as a human immunodeficiency virus-1 (HIV-1) inducible gene in human fetal astrocytes [13]. In recent years, numerous studies have revealed the essential role of AEG-1 in the

Table 1 Details of clinicopathological features, clinical outcomes, staining score, and AEG-1 expression level of all 38 patients.

Case No.	Gender	Age at diagnosis (months)	Stage	Recurrence status	Status at last follow-up	Disease free survival (months)	Overall survival (months)	Extent of staining score	Staining intensity score	AEG-1 expression level
1	Female	36	I	Yes	Dead	8	11	2	3	High
2	Male	36	II	Yes	Alive	11	123	2	2	High
3	Female	13	I	No	Alive	113	113	1	3	Low
4	Female	51	II	Yes	Dead	8	10	3	3	High
5	Male	71	I	No	Alive	107	107	3	2	High
6	Female	21	I	No	Alive	104	104	1	1	Low
7	Female	32	I	No	Alive	103	103	2	1	Low
8	Male	96	IV	Yes	Dead	3	4	3	3	High
9	Male	72	III	No	Alive	99	99	2	3	High
10	Male	42	I	No	Alive	97	97	1	2	Low
11	Male	18	I	No	Alive	95	95	2	3	High
12	Male	33	III	No	Alive	95	95	2	2	High
13	Female	18	I	No	Alive	94	94	2	1	Low
14	Male	10	III	No	Alive	90	90	1	3	Low
15	Female	48	III	Yes	Dead	5	7	3	3	High
16	Male	21	I	No	Alive	85	85	1	2	Low
17	Male	14	I	No	Alive	85	85	1	1	Low
18	Male	9	I	No	Alive	81	81	2	2	High
19	Male	3	I	No	Alive	81	81	2	1	Low
20	Female	9	II	Yes	Dead	6	10	3	2	High
21	Male	14	I	No	Alive	75	75	3	1	Low
22	Female	44	I	Yes	Alive	14	74	1	3	Low
23	Female	37	I	Yes	Dead	9	11	3	1	Low
24	Male	38	I	Yes	Alive	7	70	3	2	High
25	Male	22	I	No	Alive	69	69	2	1	Low
26	Female	37	I	No	Alive	69	69	1	1	Low
27	Male	14	II	No	Alive	67	67	1	2	Low
28	Male	30	II	No	Alive	66	66	2	2	High
29	Male	16	I	No	Alive	64	64	2	2	High
30	Female	39	I	No	Alive	64	64	2	1	Low
31	Male	7	III	Yes	Dead	1.5	2	3	3	High
32	Male	17	I	No	Alive	62	62	1	2	Low
33	Male	20	I	No	Alive	62	62	1	1	Low
34	Male	9	III	No	Alive	61	61	3	2	High
35	Male	16	I	No	Alive	61	61	2	1	Low
36	Female	101	I	No	Alive	61	61	2	1	Low
37	Male	132	II	No	Alive	60	60	1	3	Low
38	Female	6	I	No	Alive	60	60	2	2	High