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Increased SCF in Follicular Fluid and Granulosa Cells Positively Correlates With Oocyte Maturation, Fertilization, and Embryo Quality in Humans

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Abstract

Stem cell factor (SCF), which is derived from granulosa cells (GCs), plays a key role in the process of follicular development and oocyte maturation. The present study aimed to explore whether the levels of SCF in follicular fluid (FF) and GCs can be used as a potential marker for predicting oocyte developmental potential. Follicular fluid and GC samples from 150 female patients undergoing intracytoplasmic sperm injection were collected in this study. The SCF concentrations in FFs and SCF messenger RNA (mRNA) in GCs were evaluated by using enzyme-linked immunosorbent assay and real-time polymerase chain reaction, respectively. The results showed that the levels of SCF protein and mRNA were significantly associated with oocyte maturation, normal fertilization, cleavage, and embryo quality. Moreover, the levels of SCF protein and mRNA in pregnancy group were also higher than those in the nonpregnancy group. The cutoff value of SCF in FF for predicting high-quality embryo was 1.346, with a sensitivity of 57.8% and a specificity of 72.4%, and the cutoff value of SCF in GCs for predicting high-quality embryo was 6.650, with a sensitivity of 64.4% and a specificity of 78.1%. In conclusion, our results showed a positive and statistically significant relationship between SCF level and oocyte maturation, normal fertilization, cleavage, embryo quality, and clinical pregnancy. Therefore, the levels of SCF in FF and GCs might be considered as a new marker for predicting oocyte developmental potential.

Keywords

SCF, follicular fluid, GCs, oocyte developmental potential

Introduction

Stem cell factor (SCF), a cytokine growth factor, activates multiple signal pathways by binding with c-kit receptor. This effect is important in the regulation of diverse cell proliferation, differentiation, migration, and apoptosis, including melanin cells, hematopoietic stem cells, gastrointestinal Cajal interstitial cells, mast cells, and reproductive cells.[1,2] It has been reported that SCF and c-kit were expressed in granulose cells (GCs) and oocytes in human and other mammalian ovaries, respectively.[3-6] A subsequent study has found that SCF, derived from GCs, bound to oocyte c-kit receptor and stimulated phosphoinositide 3-kinase signal pathway.[7] This stimulation appears to improve the regulation of follicular development and to enhance the production of oocyte factors, which in turn facilitates the proliferation and differentiation of the surrounding GCs.[8] The cross talk between GCs and oocyte involving the interaction of SCF and c-kit receptor was relevant to the process of follicular development from the recruitment of the primordial follicle to ovulation, the formation of corpus luteum, and even the development of early embryo.[9]

In a study conducted by Hutt et al, follicles were cocultured with SCF or SCF-neutralizing antibody and the role of SCF in the development of early embryo was investigated.[10] The results showed that the mean diameter of oocytes from primordial, early primary, primary, and growing primary follicles in the mouse was increased significantly after treatment with SCF, and these effects were inhibited by treatment with SCF-neutralizing antibody.[10] Besides, SCF could exert its functions

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on embryonic development. Another in vitro study reported that cocultured mouse embryos with exogenous SCF significantly improved the cleavage and proliferation of blastomeres during mouse preimplantation embryogenesis by regulating AKT downstream genes.[11] Furthermore, it is well known that anti-Müllerian hormone (AMH), one of the most validated markers of ovarian reserve,[12,13] negatively modulates SCF expression through the cyclic adenosine monophosphate/protein kinase A pathway.[14,15] Interestingly, a more recent study presented a negative correlation between follicular fluid (FF) AMH concentration and oocyte viability.[16] The authors measured the concentration of AMH in FFs collected from patients undergoing in vitro fertilization (IVF) and demonstrated that compared with the high AMH group, the low AMH group showed significantly higher percentage of top quality oocytes, fertilization, clinical pregnancy, and embryo implantation rates,[16] which indicated a positive association between SCF expression and oocyte viability. Actually, Salmassi et al have investigated the variation of serum level of SCF during the menstrual cycle in the process of follicular maturation, ovulation, implantation, and pregnancy.[17] The authors found that SCF was produced during the whole follicular phase and was associated with folliculogenesis and the occurrence of ovulation; moreover, the serum SCF level might reflect a successful stimulation with ample follicle maturation.[17] All these results led us to hypothesize that SCF may be a potential marker of follicular maturation and be helpful for predicting oocyte viability.

Therefore, we conducted a study with the aim of evaluating whether the variation in SCF levels could be a new biomarker for predicting oocyte developmental potential. In this study, we measured the levels of SCF protein in FFs and SCF messenger RNA (mRNA) in GCs from patients undergoing intracytoplasmic sperm injection (ICSI) treatment and analyzed the relationship between the variation of SCF levels and oocyte developmental potential.

Methods

Patients

From December 2015 to July 2016, 150 women who received ICSI because their husbands were diagnosed as having severe oligospermia and asthenospermia were enrolled. They were in good physical and mental condition. The inclusion criteria for all patients included a super-long protocol for ovarian stimulation, age $\leq$37 years, body mass index (BMI) of 15 to 35 kg/m^2, and basal follicle-stimulating hormone (FSH) level of $\leq$15 IU/L. Women with a history of the following procedures or disorders were excluded: ovarian surgery, radiotherapy or chemotherapy, premature ovarian failure, ovarian dysfunction, adenomyosis, polycystic ovarian syndrome, thyroid dysfunction, recurrent implantation failure (failed to achieve a pregnancy after 3 or more cycles), submucosal fibroids, intrauterine adhesion, congenital uterine malformation, hydrosalpinx, and ovarian endometriomas $\geq$3 cm in diameter.

Controlled Ovarian Stimulation

Ovarian stimulation was performed with the use of a super-long protocol. Briefly, standard full dose of gonadotropin-releasing hormone agonist (3.75 mg; Ipsen, Boulogne-Billancourt, France) was used in the second day of menstrual cycle for downregulation. According to the patient's age, BMI, serum basal FSH levels, luteinizing hormone levels, estradiol levels, and antral follicle count, initial doses of 75 to 112.5 IU/d of recombinant human FSH (Merck Serono, Darmstadt, German) were used. The time and dose of recombinant human FSH were adjusted according to ovarian response as monitored by serum estradiol levels and vaginal ultrasound. When the dominant follicle was $\geq$19 mm in diameter or at least 3 follicles were $\geq$17.5 mm in diameter, recombinant human FSH was stopped and a single injection of 6000 to 8000 IU of human chorionic gonadotropin (Merck Serono) was administered. Oocyte retrieval was performed 36 to 40 hours later under transvaginal ultrasound guidance.

Follicular Fluid Collection

For the 150 patients, the follicles visualized by ultrasound were aspirated individually without flushing at the day of oocyte retrieval (n = 473). The FF samples were immediately centrifuged at 3000 rpm for 10 minutes. Supernatants were aspirated, divided into aliquots, and frozen at -80°C for future analysis. Any FF sample that was not clear or showed obvious contamination with blood was discarded.

Enzyme-Linked Immunosorbent Assay for SCF Measurements

Concentration of SCF in each FF sample was determined with a commercially available enzyme-linked immunosorbent assay (ELISA) kit (R&D Systems, Minneapolis, Minnesota). All of the procedures were performed according to the previous study.[15]

Human GC Collection

Only the GCs from the collected follicles were collected. Two hours after ovum pickup, GCs surrounding the oocyte were stripped. Granulosa cells were collected and dispersed under a dissecting microscope, then centrifuged at 3000 rpm for 5 minutes, washed twice in phosphate-buffered saline, and resuspended with the density of 1×10^5 cells. For real-time polymerase chain reaction (PCR), the cells were mixed with TRIzol and reserved at -80°C.

RNA Extraction and Real-Time PCR

Total RNA was extracted from GCs with RNeasy kit (Qiagen, Beijing, China), according to the manufacturers' instructions. Reverse transcription reactions were performed using Super cDNA First-Strand Synthesis Kit (CWBiotech, Beijing, China). Real-time PCR was performed in an ABI 7500 real-time PCR system (Applied Biosystem, Carlsbad, California) using Ultra

SYBR Mixture with ROX (CWBiotech). The following primers were used: SCF (forward: CAGAGTCAGTGTCACAAAAC CATT, reverse: TTGGCCTTCCTATTACTGCTACTG) and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) (forward: AGAAGGCTGGGGCTCATTTG, reverse: AGGGGCCATCCA CAGTCTTC). The reactions were incubated at 95°C for 10 minutes, followed by 40 cycles at 95°C for 15 seconds and at 60°C for 1 minute. All reverse transcription reactions included no-template controls; and all PCR reactions were run in triplicate.

Quartile Model

Quartiles (Q) of SCF level measured in the FF and GC (n = 473) samples of the 150 patients were defined as follows, respectively:

SCF in FF (ng/mL):
- Q1 (<0.739)
- Q2 (≥0.739, <1.024)
- Q3 (≥1.024, <1.568)
- Q4 (≥1.568)

SCF in GCs:
- Q1 (<3.45)
- Q2 (≥3.45, <5.1)
- Q3 (≥5.1, <7.7)
- Q4 (≥7.7)

Statistical Analysis

The mean (SD) and 95% confidence intervals were reported for quantitative data and percentages for categorical ones. Covariance analysis was used to compare SCF level in different groups after adjusting for age. Univariate logistic regression was used to estimate the effect of SCF levels on oocyte developmental potential after adjusting for age. For each parameter, we compared the model including SCF level as a continuous variable with the model including SCF level quartiles as qualitative variables to select and report the best one. The first quartile (Q1) was taken as the reference for the comparison with the other quartiles. Then, prognostic effect of patient's characteristics on oocyte developmental potential was estimated using univariate logistic regression models. For all these logistic regression models, robust variance estimations for cluster correlated data were used. Receiver operating characteristic (ROC) curves were used to examine the diagnostic value of SCF in FF and GCs for predicting high-quality embryo. The area under the curve represents the probability of correctly identifying the high-quality and non-high-quality embryos. Data analysis was conducted with SPSS 17.0, and $P < .05$ was considered as statistically significant.

Results

General Conditions

The general characteristics of all the patients enrolled in this study are summarized in Table 1.

Table 1. The General Conditions of All Patients.

General Indicators	Value (Standard deviations)
No. of case	150
No. of collecting OGCs	473
Age (years)	29.83 (4.66)
BMI (kg/m^2)	22.46 (3.79)
Basal FSH (IU/L)	6.72 (2.55)
Basal LH (mIU/mL)	8.67 (4.58)
Basal E_2 (pg/mL)	41.86 (37.52)
PRL (pg/mL)	17.60 (7.61)
T (ng/dL)	36.7 (18.54)
Gn dosage (IU)	2472.97 (1152.97)
Days of stimulation	11.99 (2.18)

Abbreviations: E_2, estradiol; FSH, follicle-stimulating hormone; Gn, gonadotropin; LH, luteinizing hormone; OGCs, oocyte–granulosa cell complexes; PRL, prolactin; T, testosterone.

Correlation Between the Concentration of SCF in FF and Oocyte Developmental Potential

Amount of SCF was detected in 473 individual FF samples from 150 female patients. First, we divided SCF concentration into quartiles (Table 2) and found significant associations between SCF concentration in FF and the oocyte maturation, normal fertilization, cleavage, and embryo quality ($P < .01$, $P < .01$, $P < .01$, $P < .01$, respectively). Furthermore, if SCF concentrations were greater than or equal to 0.739 ng/mL (including Q2, Q3, and Q4), the rate of MII oocyte, normal fertilization, cleavage, and high-quality embryo was significantly increased (odds ratio [OR]: 5.0, 3.9, and 7.5; OR: 7.9, 10.1, and 8.3; OR: 10.9, 8.7, and 12.8; OR: 2.8, 4.7, and 12.8 in Q2, Q3, and Q4, respectively).

Correlation Between the Expression of SCF in GCs and Oocyte Developmental Potential

Then, we detected SCF mRNA expression in GCs from 473 individual oocyte–GC complexes from 150 female patients. Likewise, when considering SCF expression divided into quartiles (Table 3), we also found that the expression of SCF in GCs was significantly associated with the oocyte maturation, normal fertilization, cleavage, and embryo quality ($P < .01$, $P < .01$, $P < .01$, $P < .01$, respectively). Moreover, if SCF expressions were above 3.45, the rate of MII oocyte, normal fertilization, cleavage, and high-quality embryo was significantly elevated (OR: 1.7, 3.1, and 7.5; OR: 8.9, 9.1, and 11.6; OR: 5.6, 7.7, and 9.0; OR: 4.5, 4.3, and 7.1 in Q2, Q3, and Q4, respectively).

Comparison of the Levels of SCF in FF and GCs Between the Groups With and Without High-Quality Embryos

The average levels of SCF in FF and GCs in the group with high-quality embryos were 1.37 ± 0.49 ng/mL and 6.64 ±

Table 2. Probabilities of SCF Concentration in Human FF to Predict Oocyte Developmental Potential.[a]

SCF Quartiles (ng/mL)	n/Number of FF Analyzed (%)	*P*	OR (95% CI)	*P*
Probabilities of obtaining MII oocytes				
Q1 (<0.739)	68/119 (57.1%)	<.01	- (Reference)	
Q2 (≥0.739, <1.024)	101/118 (91.5%)		5.0 (2.04-9.21)	<.01
Q3 (≥1.024, <1.568)	111/117 (94.9%)		3.9 (3.29-10.11)	<.05
Q4 (≥1.568)	111/119 (93.3%)		7.5 (1.98-12.74)	<.05
Probabilities of obtaining 2PN oocytes				
Q1 (<0.739)	57/119 (47.9%)	<.01	- (Reference)	
Q2 (≥0.739, <1.024)	89/118 (75.4%)		7.9 (3.29-23.61)	<.01
Q3 (≥1.024, <1.568)	96/117 (82.1%)		10.1 (1.98-16.14)	<.01
Q4 (≥1.568)	105/119 (88.2%)		8.3 (2.04-19.21)	<.01
Probabilities of obtaining cleavage oocytes				
Q1 (<0.739)	37/119 (31.1%)	<.01	- (Reference)	
Q2 (≥0.739, <1.024)	65/118 (55.1%)		10.9 (1.31-23.18)	<.01
Q3 (≥1.024, <1.568)	69/117 (59.0%)		8.7 (0.98-15.74)	<.01
Q4 (≥1.568)	86/119 (72.3%)		12.8 (8.21-17.71)	<.01
Probabilities of obtaining high-quality embryos				
Q1 (<0.739)	12/119 (10.1%)	<.01	- (Reference)	
Q2 (≥0.739, <1.024)	25/118 (21.2%)		2.8 (0.68-7.22)	<.05
Q3 (≥1.024, <1.568)	33/117 (28.2%)		4.7 (1.28-12.53)	<.01
Q4 (≥1.568)	37/119 (31.1%)		12.8 (1.60-18.87)	<.01

Abbreviations: CI, confidence interval; FF, follicular fluid; MII, maturation rate; 2PN, normal fertilization rate; OR, odds ratio; SCF, stem cell factor.
[a]Probabilities of SCF concentration in human FF were divided into quartiles (Q): Q1, quartile 1; Q2, quartile 2; Q3, quartile 3; Q4, quartile 4. Q1 was considered as the reference.

Table 3. Probabilities of SCF mRNA Expression in Human GCs to Predict Oocyte Developmental Potential.[a]

SCF Quartiles	n/Number of Follicles Analyzed (%)	*P*	OR (95% CI)	*P*
Probabilities of obtaining MII oocytes				
Q1 (<3.45)	68/119 (59.1%)	<.01	- (Reference)	
Q2 (≥3.45, <5.1)	105/118 (89.0%)		1.7 (1.20-2.38)	<.01
Q3 (≥5.1, <7.7)	105/117 (90.0%)		3.1 (2.09-4.89)	<.01
Q4 (≥7.7)	113/119 (95.0%)		7.5 (1.08-2.54)	<.01
Probabilities of obtaining 2PN oocytes				
Q1 (<3.45)	60/119 (50.4%)	<.01	- (Reference)	
Q2 (≥3.45, <5.1)	92/118 (78.0%)		8.9 (1.29-13.11)	<.01
Q3 (≥5.1, <7.7)	94/117 (80.1%)		9.1 (2.02-9.84)	<.01
Q4 (≥7.7)	100/119 (84.0%)		11.6 (4.74-20.01)	<.01
Probabilities of obtaining cleavage oocytes				
Q1 (<3.45)	30/119 (25.2%)	<.01	- (Reference)	
Q2 (≥3.45, <5.1)	70/118 (59.3%)		5.6 (1.31-13.02)	<.01
Q3 (≥5.1, <7.7)	76/117 (65.0%)		7.7 (6.02-15.74)	<.01
Q4 (≥7.7)	81/119 (68.1%)		9.0 (0.11-19.87)	<.01
Probabilities of obtaining high-quality embryos				
Q1 (<0.739)	10/119 (8.4%)	<.01	- (Reference)	
Q2 (≥0.739, <1.024)	30/118 (25.4%)		4.5 (1.30-15.41)	<.05
Q3 (≥1.024, <1.568)	32/117 (27.4%)		4.3 (1.28-14.53)	<.01
Q4 (≥1.568)	36/119 (30.1%)		7.1 (2.13-23.79)	<.01

Abbreviations: CI, confidence interval; GCs, granulosa cells; mRNA, messenger RNA; MII, maturation rate; 2PN, normal fertilization rate; OR, odds ratio; SCF, stem cell factor.
[a]Probabilities of SCF mRNA expression in human GCs were divided into quartiles (Q): Q1, quartile 1; Q2, quartile 2; Q3, quartile 3; Q4, quartile 4. Q1 was considered as the reference.

2.04, respectively, while these levels in the group without high-quality embryos were 1.02 ± 0.53 ng/mL and 5.04 ± 2.67, respectively. Compared with the group without high-quality embryos, the group with high-quality embryos showed significantly higher levels of SCF in FF and GCs ($P < .01$, $P < .01$, respectively; Figure 1).

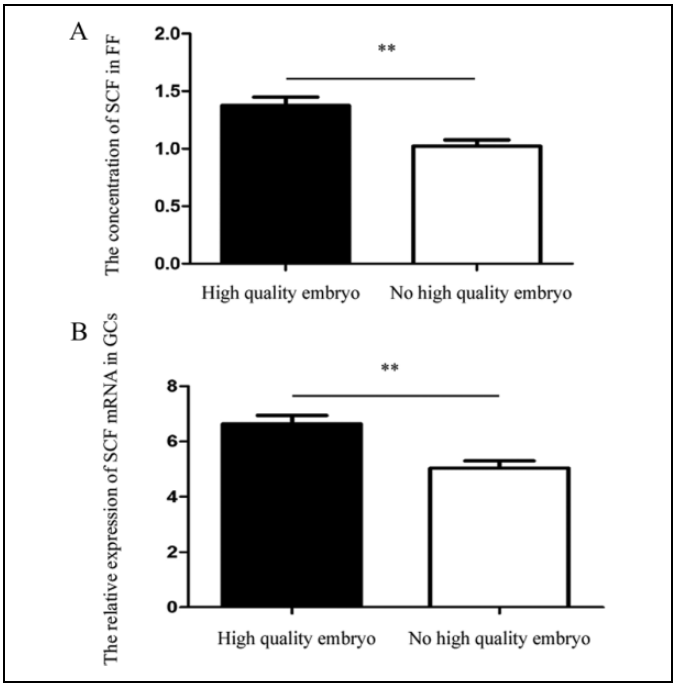

Figure 1. Comparison of the levels of stem cell factor (SCF) protein and messenger RNA (mRNA) between the groups with and without high-quality embryos. A, The concentrations of SCF in follicular fluid (FF) in the groups with and without high-quality embryos (**$P < .01$). B, The relative expressions of SCF mRNA in granulosa cells (GCs) in the groups with and without high-quality embryos (**$P < .01$).

Table 4. Diagnostic Value of SCF in FF and GCs for Predicting High-Quality Embryos.

	AUC	*P*	Threshold	Sensitivity	Specificity
SCF in FF	0.675 (0.583-0.768)	<.01	1.346	57.8%	72.4%
SCF in GCs	0.688 (0.599-0.777)	<.01	6.650	64.4%	78.1%

Abbreviations: FF, follicular fluid; GCs, granulosa cells; SCF, stem cell factor.

Diagnostic Value of SCF in FF and GCs for Predicting High-Quality Embryo

The diagnostic value of SCF in FF and GCs for predicting high-quality embryo is summarized in Table 4. The area under the ROC curve of SCF in FF for predicting high-quality embryo was 0.675 (0.583-0.768), with a cutoff value of 1.346, a sensitivity of 57.8%, and a specificity of 72.4%. The area under the ROC curve of SCF in GCs for predicting pregnancy was 0.688 (0.599-0.777), with a cutoff value of 6.650, a sensitivity of 64.4%, and a specificity of 78.1%.

Comparison of the Levels of SCF in FF and GCs Between the Groups With and Without Pregnancy

The patients' characteristics are presented in Table 5. As shown in Figure 2, the levels of SCF in FF and GCs in the pregnancy group (1.35 ± 0.46 ng/mL and 6.29 ± 2.53, respectively) were remarkably greater than those in the nonpregnancy group (0.79 ± 0.44 ng/mL and 4.47 ± 2.30, respectively; $P < .01$, $P < .01$, respectively).

Table 5. Clinical Parameters of the Groups With and Without Pregnancy.[a]

General indicators	Pregnancy (Standard deviations)	Nonpregnancy (Standard deviations)	*P*
No. of case	103	47	-
Age (years)	29.91 (6.12)	30.14 (5.31)	NS
No. of collecting OGCs	341	132	-
Average SCF level in FF (ng/mL)	1.35 (0.46)	0.79 (0.44)	<.01
Average SCF level in GCs	6.29 (2.53)	4.47 (2.30)	<.01
BMI (kg/m^2)	22.98 (2.11)	23.53 (3.01)	NS
Basal FSH (IU/L)	5.95 (3.77)	6.91 (2.69)	NS
Basal LH (mIU/mL)	9.18 (4.06)	8.71 (4.07)	NS
Basal E_2 (pg/mL)	40.35 (33.26)	49.86 (40.28)	NS
PRL (ng/mL)	15.91 (7.96)	17.99 (6.63)	NS
T (ng/dL)	33.7 (13.67)	36.68 (17.93)	NS
Gn dosage (IU)	2522.03 (980.12)	2236.95 (1189.61)	NS
Days of stimulation	11.81 (2.13)	10.97 (3.38)	NS
No. of transferred embryos	1.79 (0.63)	1.83 (0.41)	NS

Abbreviations: BMI, body mass index; E_2, estradiol; FF, follicular fluid; FSH, follicle-stimulating hormone; GCs, granulosa cells; Gn, gonadotropin; LH, luteinizing hormone; NS, not significant; OGCs, oocyte–granulosa cell complexes; PRL, prolactin; SCF, stem cell factor; T, testosterone.
[a]The pregnancy group compared with the nonpregnancy group.

Discussion

Oocyte plays an important role in IVF and embryo transfer (IVF-ET) progression. The successful rate of IVF-ET in some degree is determined by oocyte developmental potential. Thus, the precise assessment of oocyte developmental potential is an important issue in the process of IVF-ET. In the present study, we detected the levels of SCF in FF and GCs from patients undergoing ICSI by using ELISA and real-time PCR, respectively. The relationship between the levels of SCF and oocyte viability was investigated in order to explore new biomarkers for embryo selection.

It has been proved that SCF plays an essential role in human reproduction.[9] Inhibition of SCF/c-kit system disrupts the primordial follicular development, primary follicle growth, FF formation of preantral follicles, and the ovulation of mature follicles in vivo.[18] Inversely, cocultured mouse oocytes with exogenous SCF remarkably promoted first polar body extrusion of mouse preovulatory oocytes.[19] Here, we found that the levels of SCF in FF and GCs were positively associated with oocyte developmental potential. Our study showed that with the increasing SCF level, the oocyte maturation rate also elevated significantly. Actually, similar results have been found in

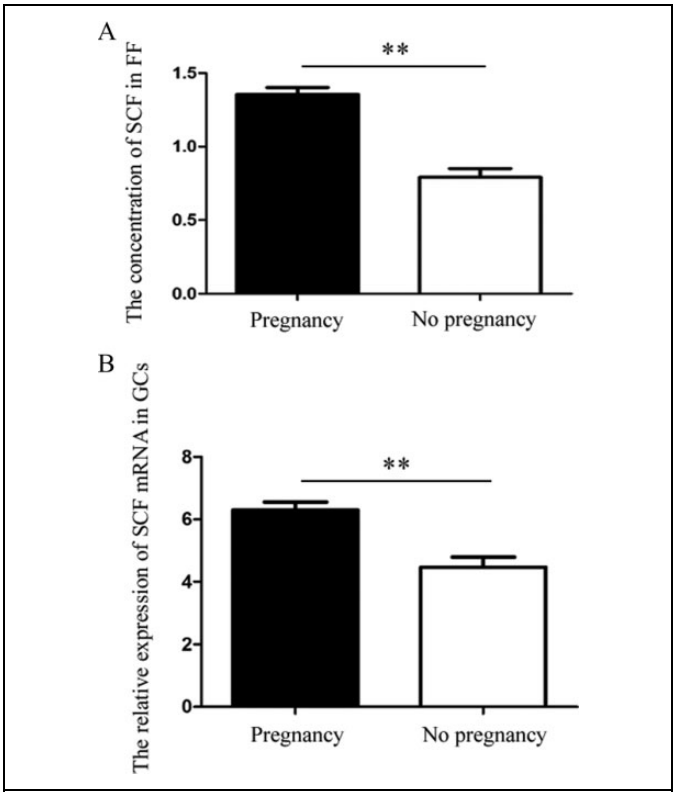

Figure 2. Comparison of the levels of stem cell factor (SCF) protein and messenger RNA (mRNA) between the groups with and without pregnancy. A, The concentrations of SCF in follicular fluid (FF) in the groups with and without pregnancy (**$P < .01$). B, The relative expressions of SCF mRNA in granulosa cells (GCs) in the groups with and without pregnancy (**$P < .01$).

recent study. Gizzo et al[20] have detected the levels of SCF in serum and FF from the elderly poor responder patients undergoing IVF. The results demonstrated that the SCF concentrations in serum and FF were positively correlated with MII oocytes rate.[20] All these findings imply that the levels of SCF in FF and GCs might reflect oocyte viability.

It is well known that oocyte viability is an important factor to impact the process of normal fertilization, cleavage, and subsequent embryonic development.[21,22] Generally, high-quality oocytes with better function more easily develop into high-quality embryos than low-quality oocytes with imperfect function.[23] Several studies have documented that high expression of some factors within oocyte–GC complex, such as apolipoprotein B, growth differentiation factor 9, and bone morphogenetic protein 15, significantly increased the embryo cleavage rate and improved the embryonic quality.[24,25] These evidences help to explain our findings that the levels of SCF in FF and GCs from the group with high-quality embryos were significantly greater than those from the group without high-quality embryos. As known, another important indicator for evaluating embryo quality is clinical pregnancy. Although the clinical pregnancy outcome is determined by several factors such as the microenvironment of uterine endometrium and sperm quality, the oocyte quality is the most important factor for clinical pregnancy outcome. A high-quality oocyte often has more chances of developing into high-quality embryo, which is beneficial to pregnancy.[26] Smikle et al[27] have detected the SCF concentrations in FF from patients undergoing IVF and analyzed the association between the FF concentration of SCF and clinical outcomes. The authors found that high clinical pregnancy was often accompanied with high concentration of SCF in FF,[27] suggesting that increased SCF concentration in FF might improve pregnancy rate after oocyte retrieval, fertilization, and embryo transfer. Interestingly, Hammadeh et al[28] evaluated the relationship between SCF level in FF and ICSI outcome and obtained contradictory results with our study. The authors stated that ICSI outcome was not related to SCF concentrations in serum or FF, and therefore, this parameter could not be used as a prognostic factor in ICSI program.[28] In their study, the authors pooled the FF samples together and detected the average SCF concentration from the whole FF, instead of each FF sample. It is hard to investigate the relationship between the SCF concentration and each oocyte and/or embryo quality. Therefore, it is possible that the patient presented high average SCF concentration in all FF samples but transplanted with lower quality embryo, which leaded to pregnancy fail. In our study, we compared the SCF level and the quality of each oocyte or/and embryo, then transplanted the embryos with higher SCF level. The results showed that the levels of SCF in FF and GCs from the pregnancy group were significantly greater than those from the nonpregnancy group. These findings suggest that increased SCF levels in FF and GCs might be contributed to oocyte development, which was beneficial to pregnancy. As the ROC curve was used to evaluate the diagnostic value of SCF in FF and GCs, the cutoff value can be established for predicting oocyte viability with a relatively high sensitivity. These data indicate that the detection of SCF in FF and GCs may have broad application prospects as noninvasive biomarkers for evaluating oocyte developmental potential.

Conclusion

The levels of SCF in FF and GCs were significantly related to oocyte maturation, normal fertilization, cleavage, embryo quality, and clinical pregnancy outcome. Therefore, the levels of SCF in FF and GCs may be considered as new biomarkers for predicting oocyte developmental potential.

Authors' Note

The present study was approved by the Clinical Ethical Committee of Jiangxi Provincial Maternal and Child Health Hospital, and informed consents from patients were obtained before the initiation of the study.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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