Patients with ovarian carcinoma excrete different altered levels of urine CD59, kininogen-1 and fragments of inter-alpha-trypsin inhibitor heavy chain H4 and albumin

Siti S Abdullah-Soheimi1, Boon-Kiong Lim2, Onn H Hashim3,4, Adawiyah S Shuib1,4*

Abstract

Background: Diagnosis of ovarian carcinoma is in urgent need for new complementary biomarkers for early stage detection. Proteins that are abnormally excreted in the urine of cancer patients are excellent biomarker candidates for development of new noninvasive protocol for early diagnosis and screening purposes. In the present study, urine samples from patients with ovarian carcinoma were analysed by two-dimensional gel electrophoresis and the profiles generated were compared to those similarly obtained from age-matched cancer negative women.

Results: Significant reduced levels of CD59, kininogen-1 and a 39 kDa fragment of inter-alpha-trypsin inhibitor heavy chain H4 (ITIH4), and enhanced excretion of a 19 kDa fragment of albumin, were detected in the urine of patients with ovarian carcinoma compared to the control subjects. The different altered levels of the proteins were confirmed by Western blotting using antisera and a lectin that bind to the respective proteins.

Conclusion: CD59, kininogen-1 and fragments of ITIH4 and albumin may be used as complementary biomarkers in the development of new noninvasive protocols for diagnosis and screening of ovarian carcinoma.

Background

Ovarian carcinoma is the leading cause of death among gynaecologic malignancy. It is the fourth most common cancer affecting women in Malaysia [1]. Patients with ovarian carcinoma often presented themselves at an advance stage of cancer mainly because of the lack of biomarker for early diagnosis and that the cancer is usually asymptomatic at the early stages [2]. Once the cancer is detected at the advance stage, the five-year survival rate of the patients decreases to 25% even when appropriate treatments were provided [3,4].

The gel-based proteomic analysis provides a convenient method to compare the levels of proteins in bodily fluid samples. In the search for new protein biomarker candidates with clinical diagnostic value, substantial progress has been made in the proteomic analysis of serum samples of patients with different cancers [5-7].

In contrast, fewer studies have been carried out on the urine samples of cancer patients. This is despite that urine is generally a better sample for investigative and screening purposes and that the use of urine protein biomarkers such as albumin and human chorionic gonadotropin for clinical diagnosis has been a long standing practice.

The proteomic analysis of urine offers ample opportunities for clinical translation [8,9]. To date, proteomic experiments that have been conducted on urine were not confined to patients suffering from diseases of the genitourinary system [10] but were also carried out on those with atherosclerosis [11], sleep disorder [12] and cancers of the bladder [13], pancreas [14,15], lung [16] and colon [17]. Proteomic investigation has been performed on urine of patients with ovarian carcinoma but is currently restricted to the low molecular weight peptide analysis using the SELDI-TOF-MS approach [18].

In the present study, urine protein samples from patients with ovarian carcinoma and cancer negative women were subjected to the conventional two-dimensional