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JOURNAL ARTICLE

Measurement of prostate-specific antigen and human glandular kallikrein 2 in different body fluids

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It has been demonstrated that prostate-specific antigen (PSA), in spite of its name, can be detected in body fluids and tumors from a variety of organs. Investigations have shown that human glandular kallikrein 2 (hK2), a related prostate-secreted protease, can activate the zymogen form of PSA, suggesting that the two enzymes might work as a functional unit, with hK2 as the activator molecule and PSA as the effector molecule. If this is true, then hK2 should be found together with PSA in body fluids other than seminal plasma, as well. Recently, a sensitive and specific assay was devised for hK2, enabling its measurement in picogram quantities. With this assay, the concentration of hK2 was determined in samples of seminal plasma, amniotic fluid, breast milk, and saliva. Simultaneously, the samples were assayed for molecular forms of PSA. In seminal plasma, the mean PSA concentration was 0.82 mg/ml, while the hK2 level was around two orders of magnitude lower: mean value, 6.4 microg/ml. Approximately the same ratio of PSA to hK2 as in seminal plasma was found in amniotic fluid and breast milk, but in most samples, the hK2 values were too low for direct measurements and had to be concentrated prior to analysis. Measurable levels of PSA, all in the free form, were detected in amniotic fluid at the thirteenth week of gestation and then gradually increased to levels around and over 1 microg/L from the twentieth week. Significant levels of PSA were detected in amniotic fluid collected at delivery, also. Measurable levels of mammary PSA were primarily detected in colostrum, with a range from less than 0.03 microg/L to 2.1 mg/L. Around half of the molecules were in complex with protease inhibitor. Most surprisingly, determinations on saliva samples showed that none of them had detectable PSA levels but had measurable concentrations of hK2 with a mean value, 0.09 microg/L. The presence in saliva suggests that hK2 can be the human equivalent to one of the mouse salivary kallikreins with important biological function, like the epidermal growth factor-binding protein or the gamma subunit of nerve growth factor. However, this was ruled out, as a phylogenetic analysis showed that the human and mouse glandular kallikreins evolved independently from a common precursor after the separation of the primate and rodent lineages. In conclusion, the measurements show that in addition to the previously known secretion in seminal plasma, hK2 is secreted in amniotic fluid, breast milk, and saliva. Furthermore, the concerted expression of PSA and hK2 in seminal plasma, amniotic fluid, and breast milk suggests that the two proteases might form a functional unit but not

always as demonstrated by the sole presence of hK2 in saliva.

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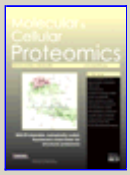

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