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tumorigenesis and metachronous second primary cancer are well-established complications in patients with cancer. multidisciplinary approaches are needed to eliminate such threats, as the risk of tumorigenesis is higher in certain locations, such as the head and neck. unfortunately, effective, novel prevention and surveillance approaches that are both of low cost and low risk are still lacking. we studied the mechanisms that underlie heart rate variability (hrv). first, we systematically derived a correlation matrix using digital photoplethysmography signals recorded during stress tests in the sleep laboratory of the kyoto stroke research center. we used a factor analysis method to analyze the relationships between all the indices of the correlation matrix. we then tested the best-fit model in another cohort of patients with sleep apnea. we identified key factors as summation of the total variability and variation of the diastolic and systolic periods. key factors showed a curvilinear dose-response relationship with the clinical characteristics of sleep apnea. in addition, the key factors independently predicted cardiovascular disease in another cohort of patients with sleep apnea. sertoli cells play an essential role in spermatogenesis by providing structural and functional support to the germ cells (cell. 4156). leydig cells and sertoli cells are the two cell types that actively secrete testosterone in mammals. testosterone plays a key role in the development of secondary sexual characteristics, such as an elongated phallus in males and the growth of breast tissue in females. the concentration of testosterone in the testis is increased during development and differentiation of the cells within the testis. in mammals, testosterone is produced from cholesterol in a sequence of three reactions, catalyzed by steroidogenic enzymes. first, the conversion of cholesterol to pregnenolone is catalyzed by hmg-coa synthase, and is the first step of a three-step pathway. second, p450scc catalyzes the conversion of pregnenolone to progesterone, which is then processed by cyp11a1 to form 17,20beta-hydroxypregnenolone, or 17,20alpha-hydroxypregnenolone. finally, 17alpha-hydroxylase (or 17,20lyase) catalyzes the conversion of 17,20alpha-dihydroxypregnenolone to testosterone (which is also termed dehydroepiandrosterone). in other organisms, the steps are catalyzed by different enzymes, and the steroidogenic pathway in species outside of mammals is much simpler and differs significantly from that of mammals. one example is in zebrafish, where cyp11b1 catalyzes the conversion of cholesterol to pregnenolone, which is then converted to 11,17alpha-dihydroxyprogesterone by p450scc (maiorino et al. 2008). the amphibian *xenopus laevis* is thought to contain homologs of all three steroidogenic enzymes. (1) cyp11b1, cyp19a1, and hsd17b7 (2) hmg-coa synthase, p450scc, and cyp17a (3) 17alpha-hydroxylase, 17beta-hydroxysteroid dehydrogenase type iv (class iii), and p450c17

routine histopathologic analyses of the right eyes and left kidneys were performed from the time of euthanasia to document the presence and extent of cardiac and renal disease. hematoxylin and eosin (h&e)-stained sections from the hearts of randomly selected animals were evaluated by a board-certified veterinary pathologist. hearts were graded using a 0 to 5 scale for lesions of myocarditis according to the american heart association (aha) recommendations⁷¹⁴² and the framingham criteria⁷⁷⁷⁸. only animals that scored at least 1 (mild lesions) or 2 (moderate lesions) for aha myocarditis and at least 1 (mild lesions) or 2 (moderate/severe lesions) for framingham myocarditis were included in the study. h&e-stained slides from the kidneys were reviewed and graded by a board-certified veterinary pathologist. approximately 10 high-powered (40×) fields per slide were examined to determine the extent of interstitial fibrosis and glomerulosclerosis (if/gs). a 0 to 3 scale was used to quantitate both features, with 0 indicating no lesions, 1 indicating lesions not present in more than 10% of the observed fields, 2 indicating lesions present in more than 10% of the observed fields, but not in the majority of the fields, and 3 indicating lesions present in more than half of the observed fields in the kidney. only animals with a score of 1 or 2 for interstitial fibrosis or glomerulosclerosis were included in the study. outcomes included the following: short-term efficacy of the therapy, defined as a decrease in c-reactive protein levels within 48 hours of treatment; long-term efficacy of the therapy, defined as a reduction in risk of kd recurrence at 1 year posttreatment; and safety of the therapy, defined as no unexpected adverse events, no cardiac events, no deaths in the first 24 hours, and no mortality or morbidity during the 10-day study. 5ec8ef588b

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