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Transient transfection of BeWo cells with a truncated human endogenous retrovirus ERV3 env induces β-hCG

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Endogenous retroviral element ERV3 env is highly expressed during differentiation of villous cytotrophoblast to syncytiotrophoblast, an essential process in human placentation, two principal characteristics being intercellular fusion and production of the hormone hCG. We reported that, unlike other retroviral env regions that encode fusion proteins, ERV3 regulated the induction of the β subunit of hCG (β-hCG). The apparent biological relevance of ERV3 env was greatly diminish by a report of 2 adults with homozygous stop mutations leading to a "natural knockout" of ERV3 that was translated into a trunicated p25 molecule lacking the typical biologically active regions of exogenous or endogenous retroviral Env proteins. However, the p25 region has never been tested for capacity to induce expression of β-hCG. We cloned and inserted the entire ERV3 env open reading frame (ERV3) or the ERV3 p25 region into pCMV6-AC expression vectors (OriGene), transiently transfected BeWo cells, and monitored for levels of intracellular β-hCG by quantitative Western blot analysis, normalized to levels of actin, and data expressed as means (SD) of the ratio of β-hCG to actin of three independent experiments. β-hCG expression was not detectable in untreated BeWo (negative control) and maximum in forskolin-treated cells (positive control; 1.83 + 0.83). Transient transfection with vector alone did not affect β-hCG expression (0.07 + 0.13), whereas both ERV3 (1.14 + 0.18) and p25 (0.76 + 0.16) induced significantly (P<0.01) greater levels of β-hCG expression. Thus, ERV3 env is an atypical retroviral element with a unique trophoblast hormone regulatory site in the SU region.

Biography

Neal S. Rote completed his Ph.D. at Temple University School of Medicine and postdoctoral studies at Heidelberg University and UCLA School of Medicine. He is currently William Weir, M.D. Professor of Reproductive Biology and Professor of Pathology at Case Western Reserve University School of Medicine and Academic Vice Chair and Director of Research in the Department of Obstetrics and Gynecology, University Hospitals Case Medical Center, Cleveland, OH. He has published over 100 papers in reproductive biology, more than 60 chapters and books, been NIH-funded for more than 30 years, and served on many NIH review committees.

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