

ULTRASENSITIVE *IN VIVO* BIOASSAY DETECTS BIOACTIVE HUMAN GROWTH HORMONE IN TRANSDUCED PRIMARY HUMAN KERATINOCYTES.

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An improved body weight assay for the potency determination of human growth hormone (hGH) has been set up in "little" mice (lit/lit), a mutant derived from the C57Bl/6J strain, reaching a detection limit of the order of ~ 0.05 µg/mouse/day, a sensitivity never reported up to now, about 20-fold higher than that presented by the most sensitive *in vivo* assay: the tibia test in hypophysectomized rats or mice. This was obtained with basis on previous work, making use of these same animals, by introduction of a careful pre-assay selection and of a three daily injection schedule.

The utilization of these conditions in a 2X2 factorial assay design allowed the potency determination of recombinant DNA-derived hGH (rec-hGH) in bacterial extracts with acceptable accuracy and precision together with the greatest economy of material, being sufficient only 0.24 mg of unknown and standard hormone preparation, for a whole 10-animal assay.

The same assay set up was also used to demonstrate the *in vivo* bioactivity of hGH secreted into a culture medium from transduced human primary keratinocytes. The growth hormone curve constructed with n=8 little mice presented a highly significant correlation ($r=0.939$, $P<0.001$) and slope = 0.016g/mouse/day. It was thus possible to prove for the first time the *in vivo* bioactivity of rec-hGH secreted by transplantable human epidermal cells, utilized as an useful experimental model for somatic gene therapy.