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DIFFERENTIAL EFFECTS OF SAQUINAVIR ON GLUCOSE TRANSPORT IN A VARIETY OF CELL CULTURES.

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We have investigated the effects of the protease inhibitor [Saquinavir](#) (S) on basal and insulin-stimulated sugar transport using ^3H -deoxy-D-glucose (DG) (0.05 mM) as the transportable substrate. Several cell culture model systems, such as:

1. human fibroblasts (HF) (connective tissue),
2. the 3T3 L1 preadipocyte (3T3) (fat cell) and
3. the L6 myoblast/myotube (L6) (muscle cell), were employed.

HF were exposed to $\pm 1\mu\text{M}$ S (approximately 7-10 days). In cells not exposed to S, the insulin (667nM):control (I:C) transport ratio was $1.48 \pm .11$ while in the S-exposed group, the I:C ratio was $0.8 \pm .23$. The decreased insulin transport stimulation in the S-exposed HF was related to a significant increase (two-tailed *t*-test, $P < 0.01$, $n=4$) in basal glucose transport in the S-exposed vs control groups, respectively (1.23 ± 0.25 vs 0.76 ± 0.32 nmoles DG/mg/protein/5 min). The effect of S on similar parameters in the L6 myoblast cell line during myotube induction (5 days) was studied over 10nM to $1\mu\text{M}$ S and 67nM insulin was the stimulating dose. No differences were observed in the I:C ratios ($2.05 \pm .12$ -control to $2.2 \pm .42$ - $1\mu\text{M}$ S) over all concentrations of S used (One Way ANOVA; $P > 0.05$, $n=4$). Also, specific insulin binding was determined in all groups of L6 \pm S with no differences being observed (One Way ANOVA; $P > 0.05$, $n=4$). Subsequently, the 3T3 adipocyte was studied employing S from 10nM to $1\mu\text{M}$ during adipocyte induction (10 days). At 67nM insulin, no differences in I:C ratios or basal sugar transport rates were observed (One Way ANOVA: $P > 0.05$, $n=4$). The data indicate that cells representative of different tissues *in vivo* respond differently to the protease inhibitor S and studies of combinations of other protease inhibitors with nucleoside and/or

nonnucleoside reverse transcriptase inhibitors could help elucidate the site(s) involved in treatment-related complications in AIDS.

Keywords: AEGIS, Monosaccharide Transport Proteins, Saquinavir, Glucose, Insulin, Adipocytes, Biological Transport, Cell Line, Hypoglycemic Agents, Blood Glucose, Insulin Resistance, Glucose-6-Phosphate, Glucose-6-Phosphatase, Fibroblasts, Human, AIDS

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