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A lag in intracellular degradation of mutant α_1-antitrypsin correlates with the liver disease phenotype in homozygous PiZZ α_1-antitrypsin deficiency

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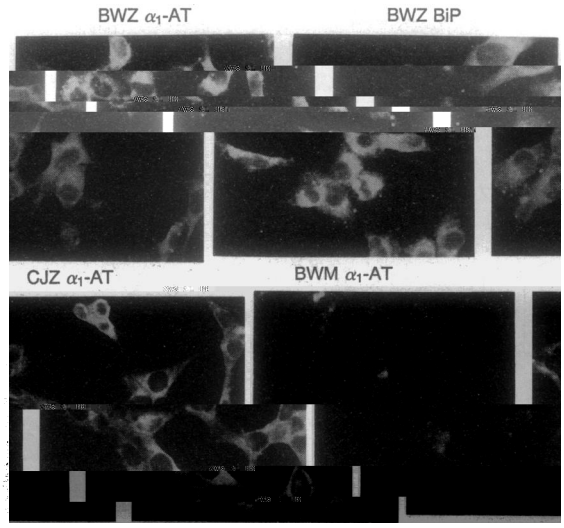
tibody to human calnexin (AF8) was provided by M. Brenner



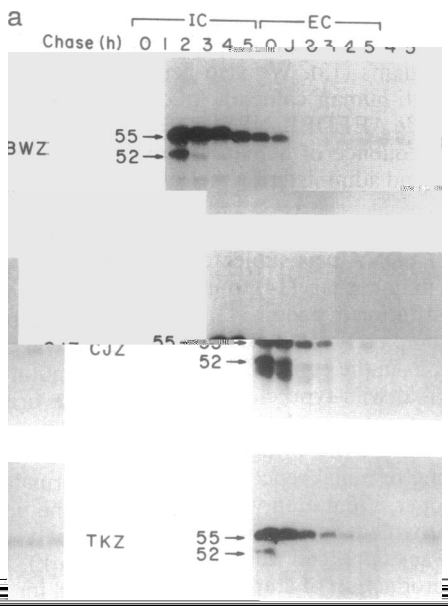
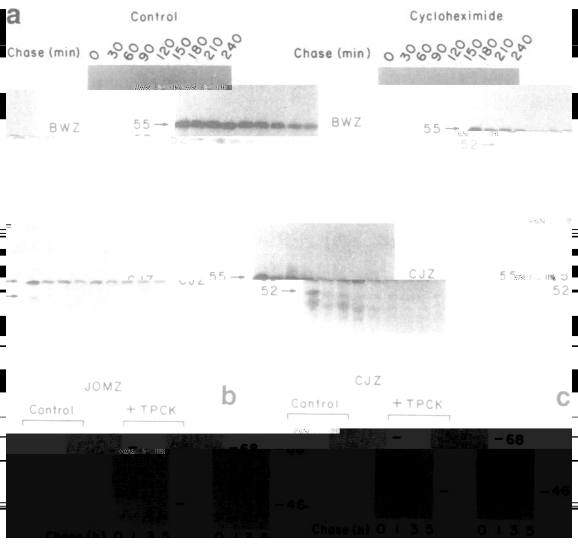


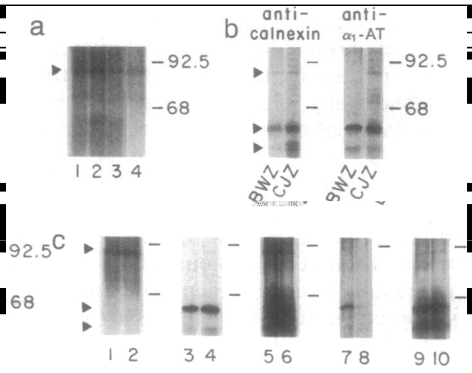
FIG. 2. Immunofluorescent staining of α_1-AT and BiP in BWZ, BWM, and CJZ cells. The cells were stained for α_1-AT or BiP and then with fluorescein isothiocyanate-conjugated anti-immunoglobulin.

were resistant to endo H. BWZ cells were also subjected to

cycloheximide on degradation of α_1-AT Z in fibroblasts from naturing conditions, to optimize coprecipitation, and the

BW (susceptible) and from CJ (protected) (Fig. 4*a*). In BWZ resulting cell lysate was subjected to immunoprecipitation in





conditions of immunoprecipitated calnexin and α_1-AT from each cell line is shown (lanes 1–4). Immunoprecipitation of calnexin (lanes 5 and 6) under nondenaturing conditions was associated with multiple bands including ones comigrating with the ~88 kDa calnexin polypeptide and ~52- and ~55-

olytic cleavage in the juxtamembrane region (29). Because we could not detect a specific proteolytic fragment of α_1-AT Z in our system, we predict that its degradation involves the major pathway for ER degradation. This would mean that the BWZ cell line is defective in this major ER degradative pathway