in B cells (but not in RL cells); the junctions became permeable to the LRB-$(Glu)_3$. The effect of serum removal in B cells had a latency of >24 hours and was completely reversible within about 24 hours of serum restoration.

One more result suggests that the channels of the two mammalian groups are not fundamentally different: when we cocultured them, the B made permeable junctions with the 3T3-BALB/c or with the lens cells. Whatever their difference, the protochannels from the membranes of the two groups still seem to pair.

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11. Growth (and test) media: Eagle-Dulbecco high-glucose (E-D) plus 10 percent fetal calf serum (FCS) for (i), (ii), (iv), and (v); E-D plus 10 percent calf serum (CS) for (vii) and (viii); BHK-2 plus 10 percent tryptose phosphate plus 10 percent CS for (ix); 199 plus 10 percent FCS for (iii); 199 plus 10 percent CS plus insulin (10 μg/ml) plus hydrocortisone (5 μg/ml) for (vi); and 199 plus Melnick's plus 2 m*M* glutamine plus 10 percent FCS for (x) and (xi). Explantation of (i) and (ii) in F-12 medium (1 day), then continued in growth medium. For coculture of (v) and (viii) we performed one experiment series with CS, another with FCS for 15 hours; heterologous junctions formed in both series.
12. The junctional transit times—the times between arrival of the probes at the injected cell boundaries and their detection in the first-order neighbors—generally ranged from 10 to 20 seconds; where junctional transfer was scored negative, observation times were at least 10 minutes. The half-times of fluorescence loss from isolated cells, recorded with a photodiode system, that images the cells through the microscope, were >30 minutes for all probes.
13. The amino acids and peptides were covalently labeled with lissamine rhodamine B (LRB) or fluorescein isothiocyanate (FITC) and purified (*5*). The 6-carboxyfluorescein (Eastman) had been introduced to biology for a different tracing function by J. N. Weinstein, S. Yoshikami, P. Henkart, R. Blumenthal, and W. A. Hagins [*Science* **195**, 489 (1977)]. We purified it by a procedure kindly communicated to us by W. Hagins; for a description, see S. J. Socolar and W. R. Loewenstein [in *Methods in Membrane Biology*, E. Korn, Ed. (Plenum, New York, 1979), vol. 10, p. 123]. Nonjunctional membrane impermeability was ascertained by bathing cultures for 0.5 hour in medium containing 5×10^{-4} *M* 6-carboxyfluorescein, FITC(Glu), LRB(Glu), $LRB(Glu)_2OH$, or $FITC(Glu)_2$ and then washing them: no fluorescence was visible in flat, well-attached cells, the only sort on which junctions were tested. "Rounded up" or loose cells, presumed to be dead or unhealthy, became fluorescent.
14. The probes were in aqueous solution (~1 m*M*) in the microelectrodes (tip, <5 μm). They were injected singly or, in some experiments (for instance, Fig. 1, I), in pairs: $LRB(Glu)_3$ and 6-carboxyfluorescein, FITC(Glu-Tyr-Glu) and LRB SO_3, $FITC(Leu)_3(Glu)_2$ and LRB SO_3. Iontophoretic currents ranged from 2.5×10^{-9} to 1×10^{-8} A.
15. The cells in *Chironomus* gland are thicker than the cultured mammalian cells and therefore the threshold for fluorescence detection is lower in the former. Thus, for the sake of comparability, we used cultured insect cells similar in size to the mammalian cells.
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19. Absolute channel bores are not assessed. The lower-limit estimate [14 to 16 Å (*5*)] given by the (nearly constant) abaxial dimensions of the present probe series is identical for mammalian and insect cells; to ascertain an upper limit (which evidently would be smaller for mammalian cells) and to refine the lower limit, one needs probes enabling one to distinguish steric from polar constraints.
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25. The frequency of permeable first-order junctions increased for LRB(Glu) from 16 to 71 percent in 3T3-42 (66 and 74 junctions tested before and after serum removal, respectively) and from 33 to 79 percent in BALB/c (90 and 135 junctions); for $LRB(Glu)_2$, from 0 to 19 percent in 3T3-42 (62 and 84 junctions) and from 0 to 36 percent in BALB/c (64 and 75 junctions); for $LRB(Glu)_3$, from 0 to 57 percent in B cells (180 junctions).
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Preferential Transmission of the Z Deficient Allele of α_1-Antitrypsin

Abstract. *The transmission of the Z deficient allele of α_1-antitrypsin was studied in 23 families, each with a single parent heterozygous for this allele. When the mother carried the Z allele, the distribution of phenotypes in the children did not differ significantly from the expected frequency. In contrast, when the father was the carrier, a significant increase of heterozygous phenotypes was observed in the children. This observation suggests that a selective advantage is associated with the expression of the Z allele in male gametes.*

α_1-Antitrypsin is the major inhibitor of protease activity in human serum (*1*). When analyzed by acid-starch gel electrophoresis, or, more recently, by isoelectric focusing, this inhibitor displays both microheterogeneity and polymorphism. The polymorphism is under genetic control, and the Pi (protease inhibitor) phenotype results from the expression of two autosomal codominant alleles in each individual (*2*). Some Pi alleles [I, P, S, W, Z, (−)] are associated with reduced serum concentrations of α_1-antitrypsin, ranging from 20 percent reduction for the I and S alleles, to 80 percent for the Z allele, and to complete absence for the "null" or (−) allele (*3*). Two major clinical disorders, pulmonary emphysema and liver diseases, have been shown to be associated with the Z allele, especially in homozygotes (*4*).

We have studied the transmission of the Z allele in 68 children from 23 families selected on the basis of the following criteria: (i) in each family, one parent had the phenotype M and the other MZ (*5*); (ii) each family included at least two children; and (iii) all the children in each family were available for investigation. The MZ parents were discovered either

Table 1. Transmission of the Z allele in children with one heterozygous parent.

Number of families	Number of children				
	Total	MM		MZ*	
		Girls	Boys	Girls	Boys
23	68	12	14	17	25

*Level of significance: $.1 > P > .05$.

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Table 2. Transmission of the Z allele according to the sex of the heterozygous parent. N.S., not significant.

Number of families	Number of children					P
	Total	MM		MZ		
		Girls	Boys	Girls	Boys	
		Father MZ				
12	41	4	6	15	16	< .01
		Mother MZ				
11	27	8	8	2	9	N.S.

in the course of population studies of volunteer blood donors or during studies of the families of homozygous Z deficient individuals.

The Pi types were determined by thin-layer isoelectric focusing in a *p*H range of 4 to 6, as previously described (*6*), and phenotypes were confirmed by print immunofixation (*6*). Concentrations of α_1-antitrypsin in the serum were determined by single radial immunodiffusion. In all subjects with apparent M phenotypes, serum values did not suggest the presence of the (−) allele in the heterozygous state (M−). The data were analyzed by the chi-square test for goodness of fit (*7*).

Analysis of Pi phenotypes in all children (Table 1), irrespective of the sex of the heterozygous parent, indicated a higher than expected number of MZ phenotypes, but this increase did not reach statistical significance. In contrast, when the families were separated according to the sex of the MZ parent (Table 2), a statistically significant increase in the number of MZ children was found ($P < .01$) in families where the father carried the Z allele. No significant departure from the expected frequency was found when the mother possessed the Z allele.

In their original study of the familial transmission of Pi phenotypes in 77 Norwegian families, Fagerhol and Gedde-Dahl (*8*) found that their inheritance was compatible with a simple autosomal codominant mode; however, their study included only five families with MM × MZ matings. In later studies, Fagerhol (*9*) and Kueppers (*10*) proposed that the Pi polymorphism is due to positive selection in favor of the variant alleles. The present results suggest a significant increase in the number of MZ children among the progeny when the father carries the Z allele in the heterozygous state. Gedde-Dahl *et al.* (*11*) have previously described another genetic abnormality associated with the Z allele in males, in that males heterozygous for the Z allele have a significantly lower frequency of recombination between Pi and the *Gm* locus (coding for immunoglobulin G heavy-chain markers) than males with other phenotypes or females heterozygous for the *Z* allele.

Our observation suggests that sperm cells carrying the Z allele have selective advantage over those carrying the M allele. Further investigations will be required to determine whether this advantage is expressed during meiosis, migration of the sperm in the female reproductive tract, or fertilization.

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Induction of Luteolysis in the Human with a Long-Acting Analog of Luteinizing Hormone-Releasing Factor

Abstract. *Subcutaneous injection of 50 micrograms of a long-acting analog of luteinizing hormone-releasing factor on each of two successive days during midluteal phase in normally cycling women induced a short luteal phase and premature menstruation. These events were associated with luteolysis, as evidenced by the consistent and parallel premature decline of progesterone and estradiol levels compared with those in control cycles. This finding may prove to be useful in the prevention or interception of implantation.*

The hypothalamic luteinizing hormone-releasing factor (LRF) is indispensable in follicular maturation, ovulation, and the maintenance of corpus luteum function (*1*). However, recent studies in animals have disclosed an unexpected and paradoxical antifertility effect of large doses of the decapeptide LRF (*2*). Several potent LRF agonists have been shown to inhibit ovulation, prevent implantation, and terminate pregnancy in the rat (*3*). In one report (*4*), daily administration of an LRF agonist for 1 month also inhibited ovulation in women. However, the irregular bleeding consequent to the disturbance of normal follicular estrogen secretion represents a major complicating factor for practical use as a contraceptive.

The present study was designed to determine whether luteolysis can be induced by administration of [D-Trp^6, Pro^9 NEt]-LRF, a long-acting LRF agonist approximately 140 times as potent as LRF (*5*, *6*). Five regularly cycling women volunteered for this study, and written informed consents were obtained. The luteal phases of their menstrual cycles were monitored by basal body temperature recording and by determining daily serum levels of gonadotropin, estradiol, and progesterone (*7*) beginning on day 10 of the cycle. In the midluteal phase, a subcutaneous injection of 50 μg

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