5. SUMMARY

The studies discussed in my thesis deal with the changes, function and regulation of membrane PLs and PKC isoforms during postnatal ontogeny.

The results that we achieved can be summarized as follows:

1. The concentration of total myocardial PLs increases proportionally to ventricular growth in rats, except for the critical developmental periods just after birth and within the suckling-weaning transition, when the increase in total PL concentration is greater than that of ventricular weight. Mainly PC, PE and DPG are responsible for the elevated gain in total PLs during the early postnatal development of rat heart. The concentration of minor PLs changes modestly until d20 and remains unchanged further. The proportion of PLPC and PLPE decreases during ontogeny, with a dramatic time course in the period just after birth and within suckling-weaning transition. ***(Supplement 1)***
2. Every PL species has its characteristic FA profile, which likely coheres with its specific structural and signaling role in cardiac membranes. Nevertheless, the FA profile of any given PL species undergoes qualitatively similar changes during postnatal ontogeny. ***(Supplement 1)***
3. The altered thyroid states induced just after birth influence the maturation of the PL component of cardiac membranes in rats during early postnatal development. Hypothyroidism decreases the concentration of PC, PE and DPG, and increases the proportion of PLPE, whereas hyperthyroidism increases the concentration of PC, PE and DPG, and decreases the proportion of PLPE in the myocardium of 21-day-old rats as compared with euthyroid controls. The FA composition of individual cardiac

PLs also underlies the TH control. Hypothyroidism decreases the ratio of saturated/unsaturated FA in PE and increases the ratio of n-6/n-3 PUFA in PC, PE and PI; on the contrary, hyperthyroidism has opposite effect on the FA composition in these PLs. Both hypo- and hyperthyroidism decrease the ratio of 20:4n-6/18:2n-6 in the majority of PLs. ***(Supplement 2)***

4. The concentration of PLs in ventricular membranes from children with normoxemic and hypoxemic congenital heart diseases does not differ much from that observed in neonatal rats. Membranes of the atrium have a lower content of PC and PE as compared with ventricles in both hypoxemic and normoxemic groups of children. In the ventricular tissue, the concentration of PE and PS is higher in children with a hypoxemic defect; in the atrium, only the PE amount is higher as compared with normoxemic ones. ***(Supplement 3)***
5. The changes in the concentration of cardiac DAG follow a biphasic pattern during the first 10 postnatal days. It declines rapidly by d5 and then increases again. The FA profile of total DAG is rather saturated and does not significantly change in the period of study. ***(Supplement 4)***
6. The total PKC activity measured by the incorporation of ^{32}P into histone IIIS decreases transiently between d2 and d3 and again between d7 and d10 in the homogenate and cytosolic, membrane and nuclear fractions essentially in a similar manner. PKCα, PKCδ and PKCε are markedly downregulated in the early postnatal period, and the expression of PKCδ and PKCε decreases mostly between d2 and d3, whereas, that of PKCα declines gradually until d10. PKCδ and PKCε are predominantly associated with particular fractions, whereas PKCα is more in the

cytosolic fraction. In the membrane and nuclear fractions, the amount of PKCδ and PKCε decrease markedly by d3, return to or close to the initial level immediately on d5 and do not change or decrease slightly later. PKCα exhibits the changes in the nuclear fraction, but is associated with the membrane fraction by d7. In the cytosolic fraction, all isoforms tend to diminish by d10, but with the transient marked increase on d7. ***(Supplement 4)***

7. The pressure overload induced on d2 affects in particular PKCδ and PKCε in the developing heart. The constriction of the abdominal aorta provoked a marked elevation in the amount of PKCδ in the membrane fraction as soon as on d3 as compared with sham operated rats. This effect gradually diminished until d10. The cardiac PKCε associated with the membrane fraction changed essentially with the same trend during the first 10 postnatal days in the pressure-overloaded heart. ***(Supplement 5)***