miR-499 Mutation and Heart Failure (p 958)

A natural human micro RNA variant affects heart failure progression in transgenic mice, report Dorn et al.

Micro RNAs (miRs) are small non-coding RNAs that bind and suppress the expression of target messenger RNA (mRNA) transcripts. Although the target mRNA sequences to which a particular miR binds can vary considerably, the miRs themselves are highly conserved across species and between individuals. This would suggest that natural variations in miR sequences would affect their function—that is, their ability to suppress target mRNAs. Dorn et al have now identified a rare variant of the cardiac-expressed miR-499 in humans, which was present in only 2 out of 2,600 DNA samples. When expressed in transgenic mice, this miR-499 variant showed impaired suppression of some target mRNAs compared with the wild-type miR-499, whereas other targets were suppressed just as well or even more effectively. Overexpression of miR-499 is associated with heart failure and both types of transgenic mice developed the condition. Interestingly, however, mice carrying the rare variant of miR-499 showed less severe disease progression. It will be interesting to see how this and other rare variant cardiac miRs affect heart pathologies in humans.

Actin and Connexin 43 (p 978)

Gap junction protein, connexin 43, takes the slow actin train to the membrane, report Smyth et al.

Gap junctions, comprised of connexin 43 proteins, are small channels in the plasma membrane that connect heart cells and enable their synchronized contraction. The channels are continuously installed and replaced at the membrane, thus requiring a steady supply of connexins. It is known that connexin-containing vesicles travel to the membrane via microtubules. However, evidence suggests that microtubule and actin cytoskeletons cooperate in vesicle transport. Smyth et al thus asked whether connexin vesicles also travel along actin. Turns out they do. In fact, live cell imaging revealed that connexin vesicles in mouse heart cells spent the majority of their time associated with the actin cytoskeleton, and this association was essential for connexin delivery. However actin was no shuttle service. Once associated, the connexin vesicles moved very slowly and stopped often. Interestingly, the connexin–actin association was disrupted in ischemic mouse heart tissue, which might be the cause of gap junction remodeling often seen after cardiac insult, say the team. Such remodeling can cause life-threatening arrhythmias, and therefore a better understanding of the connexin–actin transport might aid the design of antiarrhythmic therapies.
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