Abstract:
Nanodiamonds (ND) serve as RNA carriers with potential for *in vivo* application. ND coatings and their administration strategy significantly change their fate, toxicity, and effectivity within a multicellular system. Our goal was to develop multiple ND coating for effective RNA delivery *in vivo*. Our final complex (NDA135b) consisted of ND, polymer, antisense RNA, and transferrin.

We aimed (i) to assess if a tumor-specific coating promotes NDA135b tumor accumulation and effective inhibition of oncogenic microRNA-135b and (ii) to outline off-targets and immune cell interactions. First, we tested NDA135b toxicity and effectiveness in tumorospheres co-cultured with immune cells *ex vivo*. We found NDA135b to target tumor cells, but also to interact with granulocytes. Then, we followed with NDA135b intravenous and intratumoral applications in tumor-bearing animals *in vivo*. Application of NDA135b *in vivo* led to the effective knockdown of microRNA-135b in tumor tissue regardless of administration. Only intravenous application resulted in NDA135b circulation in peripheral blood and urine and it decreased granularity of splenocytes. Our data showed that localized intratumoral application of NDA135b represented a suitable and safe approach for *in vivo* application of nanodiamond-based constructs. Systemic intravenous application led to an interaction of NDA135b with bio-interface, and it will need further examination regarding its safety.