

## 2G4CANCER –Green graphene/lipid nanosystems for cancer imaging and treatment

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Cancer remains a worldwide leading death cause, prompting the necessity to develop new therapeutic solutions [1]. Current cancer chemotherapeutic agents can induce toxicity, even at therapeutic doses, and become ineffective by multidrug resistance (MDR) development. Furthermore, traditional synthesis of treatment and imaging agents promote some undesirable toxicity.

Doxorubicin (DOX) is a “first-line” treatment for different types of cancer which intercalates between DNA base pairs and kills fast-growing cancer cells, while also displays toxicity in healthy tissues [2,3]. Since the first DOX-loaded liposomes were approved for cancer treatment [2], research focused on these nanocarriers to reduce toxicity to healthy tissues. However, DOX-nanodelivery systems have low therapeutic efficiency due to their limited drug loading capacity, and so, pH or ion gradients are used to massively entrap DOX in the nanocarriers' aqueous core causing aggregation. These aggregates are less effective in DNA intercalation. Furthermore, even when delivered by nanocarriers, DOX is still non-specifically distributed at non-target tissues [2]. 2G4CANCER proposes DOX conjugation with green-graphene oxide quantum dots (2G-QD@DOX), due to their potential in biological labelling, photoluminescence, photostability and biocompatibility thus enabling cancer theranostic applications. The DOX conjugates will further be encapsulated in nanostructured lipid carriers of cubosomal type for higher drug entrapment and reduced oligomerization. For comparison purposes we are also testing cubosomes prepared from hybrid combinations of lipids and polymers to further encapsulate DOX.

In summary, 2G4CANCER proposes the development of eco-friendly biosynthesis of 2G-QD, to be conjugated with DOX and encapsulated in nanostructured lipid carriers to improve biodistribution and allow bio-tracking. DOX@2G-QD nanocarriers will be further silk-coated to promote stability, while allowing conjugation with siRNA for knocking-down cancer MDR pathways. Therefore, the smart nanocarriers proposed hold a multiple concept for cancer treatment: (i) enhanced therapeutic effect, (ii) imaging for traceable drug delivery, (iii) higher selectivity (by incorporating peptides targeting HER2), and (iv) controlled drug release profile.

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